“STUDY OF MYOCARDIAL DYSFUNCTION IN CHILDREN WITH SEVERE ACUTE MALNUTRITION”

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MADRAS MEDICAL COLLEGE

CHENNAI

CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY OF MYOCARDIAL DYSFUNCTION IN CHILDREN WITH SEVERE ACUTE MALNUTRITION"** is a bonafide work done by **DR.S. SENTHIL RAJA** at Madras Medical College, Chennai in partial fulfillment of the university rules and regulations for award of **M.D., Degree in Paediatrics** (BRANCH VII) during the academic year 2012-2015.

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DECLARATION

I, Dr. S. Senthil Raja, solemnly declare that this dissertation entitled **"A STUDY OF MYOCARDIAL DYSFUNCTION IN CHILDREN WITH SEVERE ACUTE MALNUTRITION"** was done by me at Madras Medical College and Institute of Child Health and Hospital for Children, during 2012-2015 under the guidance and supervision of **DR.S.GNANASAMBANDAM.,MD.,DCH.,DM.,** This dissertation is submitted to **The Tamilnadu Dr.M.G.R Medical University** towards the partial fulfillment of requirements for the award of **M.D Degree in Paediatrics** (Branch – VII).

DR. S. SENTHIL RAJA

Date :

Place : Chennai

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INSTITUTIONAL ETHICS COMMITTEE
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CERTIFICATE OF APPROVAL

To

Dr.S.Senthil Raja,
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Dear **Dr. S.Senthil Raja,**

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "**Study of Myocardial Dysfunction in children with Severe Acute Malnutrition**" No.20042014.

The following members of Ethics Committee were present in the meeting held on 08.04.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. C.Rajendran, M.D,	-- Chairperson
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7.	Thiru. Govindasamy, B.A., B.L., Lawyer, Ch.	-- Lawyer
8.	Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

9/4/14

Member Secretary, Ethics Committee

VICE PRINCIPAL
MADRAS MEDICAL COLLEGE
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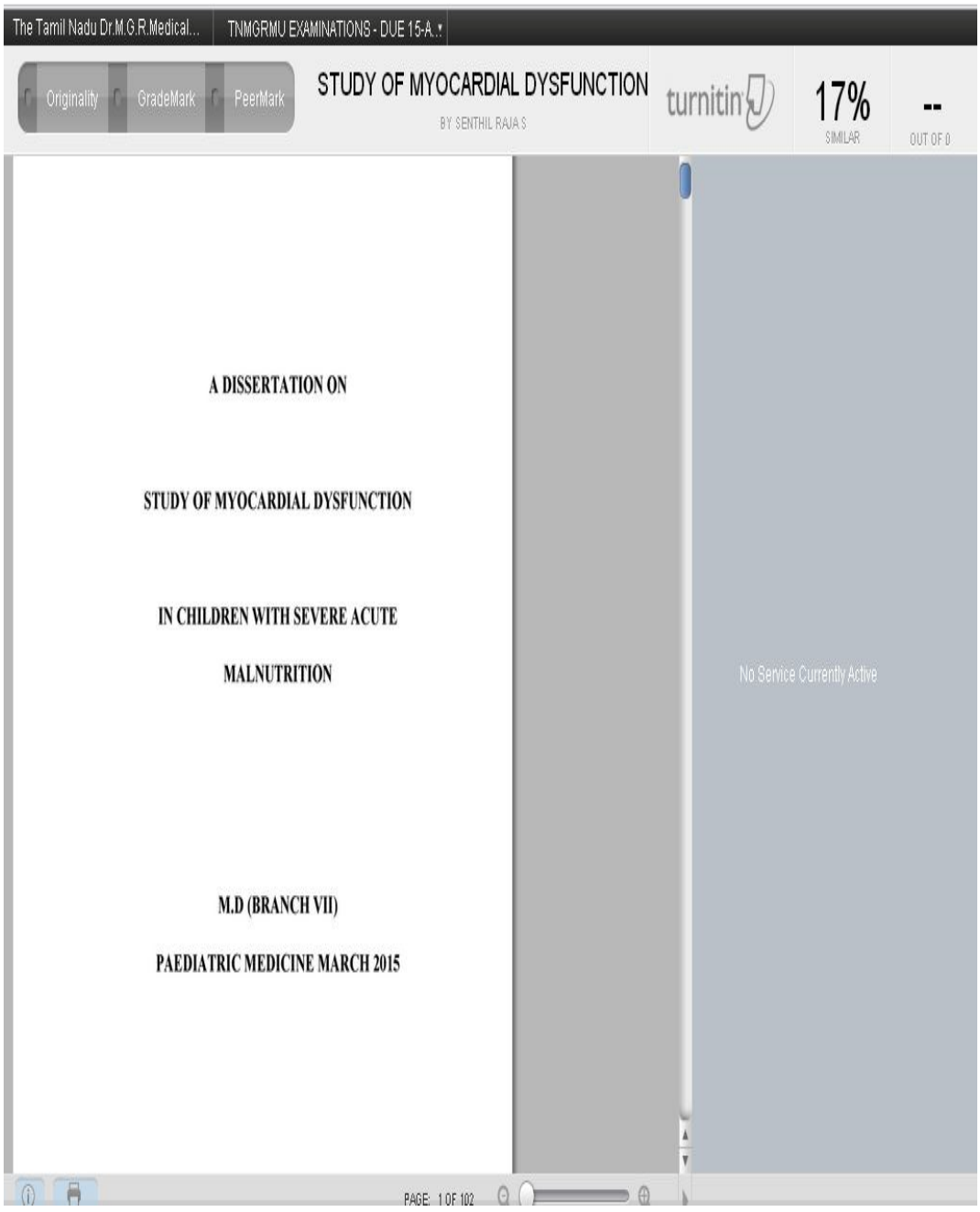
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STUDY OF MYOCARDIAL DYSFUNCTION IN CHILDREN WITH SEVERE ACUTE MALNUTRITION

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ABSTRACT

Background

Children with severe acute malnutrition suffer from several changes in the body that could produce cardiac abnormalities.

Aim

The aim of the present study was to detect the frequency of myocardial injury in children with severe acute malnutrition by echocardiography and cardiac troponin (cTnT) level.

Methods

Forty one malnourished children (mean ± SD of age was 32.41±14.95 months) were matched with twenty one apparently healthy controls (mean ± SD of age was 28.76±13.97 months). Blood sample was taken for complete blood count, liver function test, serum electrolytes and cardiac specific troponin T levels. All the malnourished children were subjected to echocardiographic evaluation.

Results

Malnourished children showed a significantly lower left ventricular (LV) mass than control group. The LV diastolic function was significantly impaired in patients with severe acute malnutrition and systolic function was not affected. Cardiac troponin T was not significantly increased in malnourished children compared to control group.

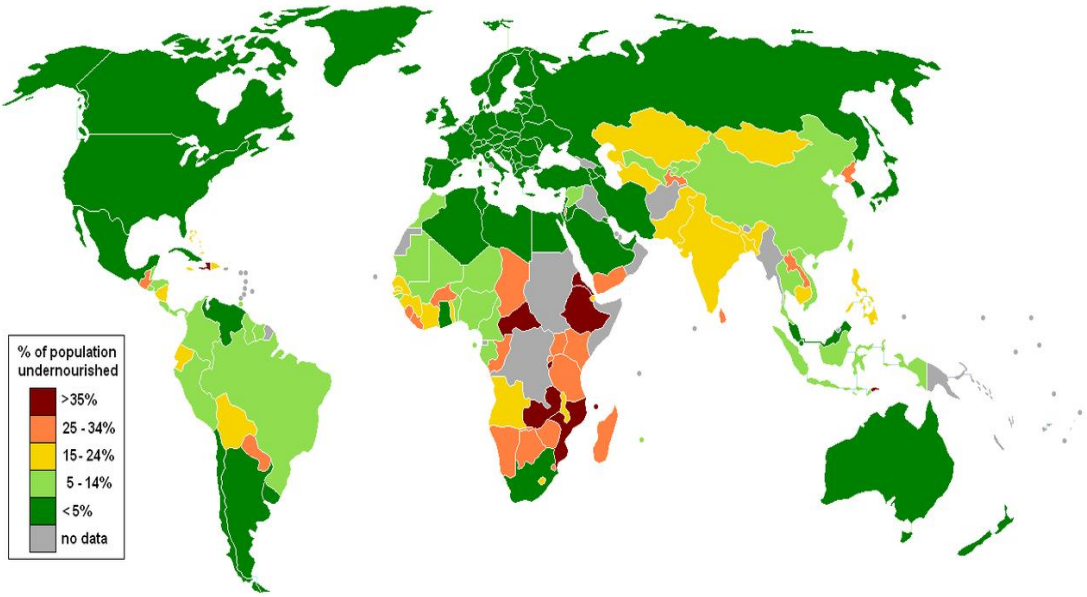
Conclusion

Children with severe acute malnutrition have significantly reduced cardiac muscle mass, diastolic dysfunction but systolic function is relatively preserved compared to control group. There is no significant difference in serum cardiac troponin T level between these two groups.

INTRODUCTION

Malnutrition is a major public health and developmental issue in India as well as other parts of the world especially in developing countries in under five age group of children. According to World Health Organization, nearly 20 million children are affected by severe acute malnutrition globally, among them most of the children live in sub-Saharan Africa and South Asia[1].

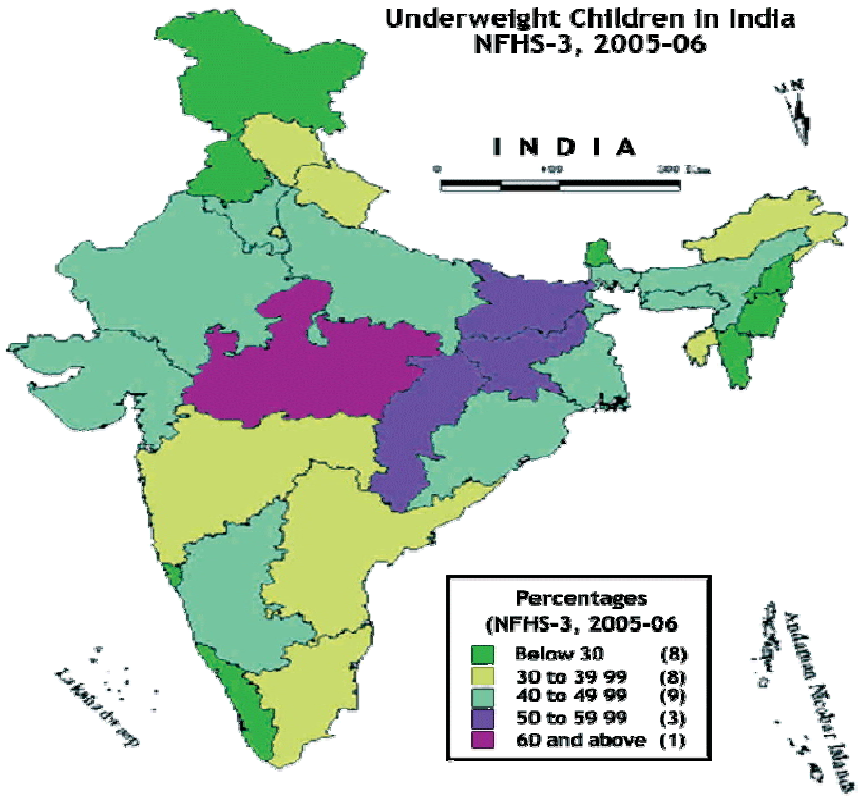
Currently 1million children die due to severe acute malnutrition every year. This mortality rate is 5-20 times more than well nourished children[2].



Global percentage of children suffering from malnutrition, 2006

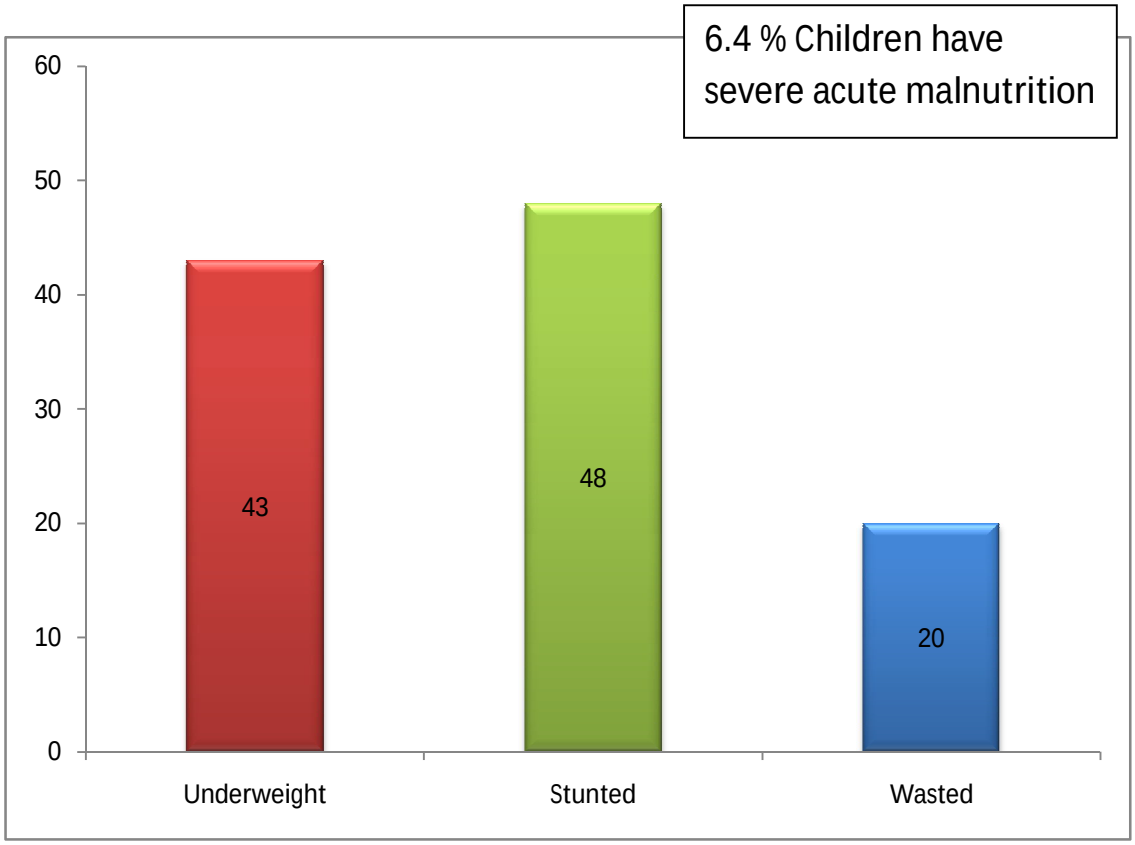
Undernutrition includes wasting (acute malnutrition), stunting (chronic malnutrition) and micronutrient deficiencies (minerals and essential vitamins).

According to National Family Health Survey-3(NFHS-3) among under five age group, 43% children are underweight (low weight for age), 48% children are stunted (low height for age), 20% children are wasted (low weight for height). Among these wasted children more than 6% are severely wasted (< -3SD) called as severe acute malnutrition[3].



NFHS-3 reported as stunted or underweight children proportion increases rapidly with child's age from birth to 20-23 months of age

attained peak at 20 months of age. Even during exclusive breastfeeding in first 6months of life, 20-30% of infants are underweight.



Prevalence of wasting, stunted, underweight, stunting among children under five years old in India (Source: NFHS 3)

Malnutrition is associated with a high rate of morbidity and mortality as it is an underlying factor in one third to half of all children under five years of age. There is a strong correlation between malnutrition and childhood mortality due to common illnesses like respiratory tract infection, diarrhea, measles and malaria.

ANTHROPOMETRY INDICES

The following three anthropometric indices are used commonly to classify undernutrition[3].

1. Weight for Age
2. Length/Height for Age
3. Weight for Length/Height

TYPES OF UNDERNUTRITION

1. UNDERWEIGHT

It is based on weight for age and is used as an overall measure of stunting and wasting. Underweight may be due to acute or chronic malnutrition or both. Weight is easily measurable so it is used as a basic indicator of the population's health status. The 'Z' score of weight-for-age at least two standard deviation below median in WHO child growth standards is considered as underweight[3].

2. STUNTING

Failure to attain expected length or height compared to well nourished healthy children of same age group is referred as stunting. It is an indicator of linear growth retardation, which is a part of growth failure. Stunting is related with chronic intake of inadequate nutrition, sustained inappropriate feeding practices, poverty and frequent infections[3].

It results in delayed development of cognition, psycho-social and poor scholastic performance. The ‘Z’ score of Height for Age is at least two standard deviation below the median in WHO child growth standard is called as stunting.

3. WASTING

Wasting is referred as recent intake of poor nutrition and is affected by recent medical illness like diarrhea and any acute illnesses. It indicates acute or current malnutrition, due to acute weight loss or failure to adequate weight gain.

The causative factors are improper feeding practices, insufficient food intake, disease or infection. However most commonly combination of these factors play a role. The ‘Z’ score of weight-for-height at least-2 standard deviation below the median in World Health Organization child growth standards is called as wasting[3].

WHO CLASSIFICATION[4]

For acute and chronic malnutrition

WEIGHT FOR AGE	HEIGHT FOR AGE	WEIGHT FOR HEIGHT	INTERPRETATION
Decreased	Decreased	Decreased	Acute on Chronic malnutrition
Decreased	Decreased	Normal	Chronic malnutrition
Decreased	Normal	Decreased	Acute malnutrition
Normal	Normal	Normal	Normal

WHO Diagnostic criteria aged 6-60 months for Severe Acute Malnutrition[3]

MEASURE	CUT-OFF	INDICATOR
Weight-for-Height	< - 3SD	Severe wasting
MUAC	< 115 mm	Severe wasting
Clinical sign	-	Bilateral edema

Reference : WHO/UNICEF joint statement

MUAC : Mid upper arm circumference

DEFINITION OF PEM

World Health Organization defined “PEM as a range of pathological conditions resulting from coincident lack of calorie and proteins in varying proportions most frequently occurring in young children and infants commonly associated with infections”.[4]

SPECTRUM OF PEM

KWASHIORKOR

The classic features are apathy, edema, stunted growth, hepatomegaly, anemia, skin and hair changes[5].

Kwashiorkor grading:

Grade I - Pedal edema

Grade II – Facial edema +Grade I

Grade III – Paraspinal and Chest edema + Grade II

Grade IV- Ascites + Grade III[5]

MARASMUS

Marasmic child has an old man appearance because of extreme wasting with just skin and bones being more prominent. Wasting initially starts in the axilla and groin followed by thigh, buttocks and chest. The buccal pad of fat is lost finally as it is metabolically least active. Brown

fat is metabolically most active with a significant role in thermogenesis, hence wasting occur first in this tissue. Marasmic child initially has good appetite and alert become irritable later[5].

MARASMIC KWASHIORKOR

When marasmic child develop edema it is termed as marasmic kwashiorkor.[5]

PATHOPHYSIOLOGY

METABOLIC RESPONSE TO INADEQUATE ENERGY INTAKE

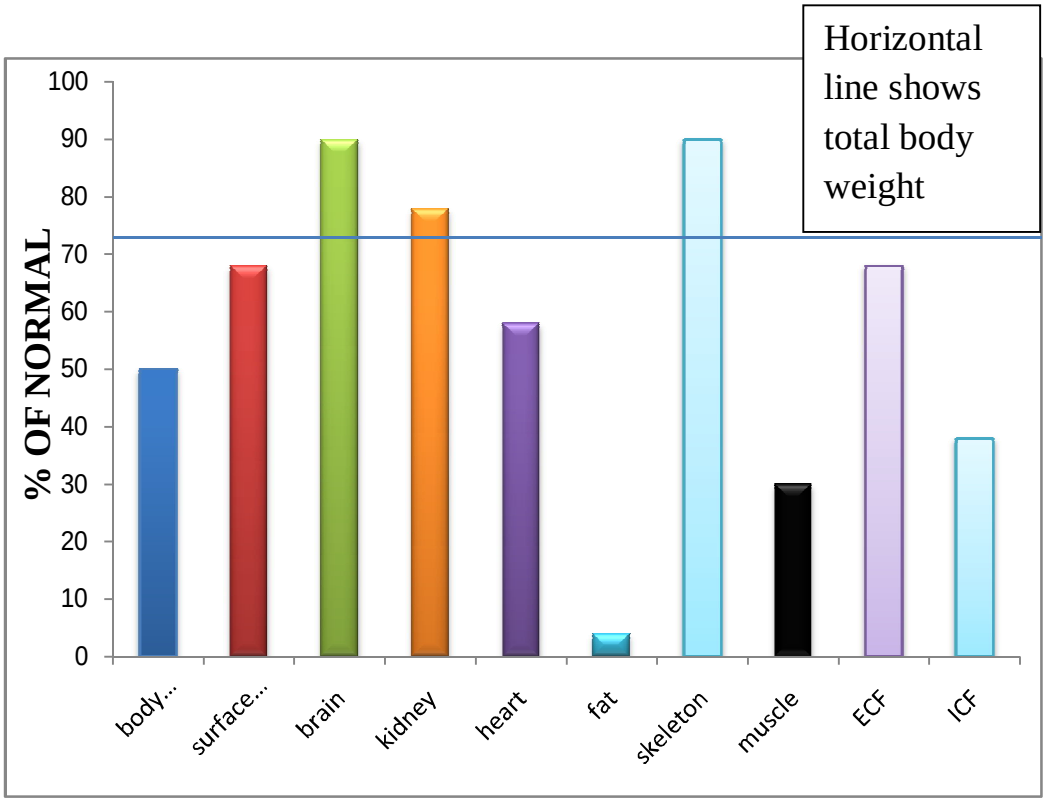
Metabolic response to insufficient calorie intake depends on many factors like age, concomitant infection, previous nutritional status of the child, nature of dietary restriction. In the absence of infection, starvation leads to fat store depletion followed by glycogen stores. These changes are mediated by endocrine and metabolic alterations that results in aim of preserving vital function, allow the child to survive till restoration of energy in the later period.

Energy expenditure in normal child[5]

ITEMS	ENERGY EXPENDITURE (%)
Basal metabolic rate (BMR)	50
Activity	25
Growth	12
Fecal loss	8
Specific dynamic action (SDA)	5

Early changes consist decreasing in activity of the child that preserves the energy expenditure. Growth is delayed, so energy need for maintaining growth is decreased and also bring down the basal metabolic rate [BMR] to conserve the energy for survival. Undernourished child have protein losing enteropathy and diarrhoea, fecal loss more compared to normal child. Depends upon type of food consumption the specific dynamic action [SDA] vary widely, SDA for carbohydrate food is low (5%), but protein rich food have very high SDA[5] (30%).

The vital organs like brain and other viscera are relatively preserved. The total body water content is increased which is mostly extracellular fluid, but intracellular fluid also increased.[6, 7]



Weights of the organ at death in atrophic children as % of normal age controls

Hormones play a major role in the metabolic adjustments to starvation. Cortisol level is increased, but stress response is maintained. The secretion of insulin into plasma is decreased leading to reduced response to glucose and peripheral insulin resistance. Due to loss of normal suppression through the glucose load Growth hormone level is increased. Insulin like growth factor -1level is reduced which is metabolic effector of the growth promoting action of Growth Hormone.

The final effects of these endocrine changes leads to fat mobilization, muscle protein degradation and decreased basal metabolic

rate. The aldosterone level is increased which cause potassium loss which is already compromised by decreased ATP synthesis on the sodium pump due to energy restriction.[8]

ADAPTATION TO REDUCED PROTEIN INTAKE

When decreased intake of protein, structural protein in the skeletal muscle is lost which is recycled to maintain essential enzymes and contribute energy for metabolic processes. The muscle protein breakdown is increased and synthesis of muscle protein decreased both occur at the same to supply essential aminoacids to the liver for gluconeogenesis and protein synthesis. In the liver transferrin, apolipoprotein B and albumin synthesis are decreased but other protein synthesis is maintained.[8]

CHANGES IN ELECTROLYTES

Sodium retention occurs in both kwashiorkor and marasmus which increases the whole body sodium leading on to increased extracellular fluid even when the serum sodium is low. The total serum potassium is decreased even serum potassium remains normal. Initially there is acute repletion of potassium during hypokalemia then reestablishment of normal sodium/potassium gradient followed by third phase increased potassium requirements during rapid growth of skeletal muscle. Nichols

and colleagues observed in their study that the amount of potassium needed in the first week or during acute phase of recovery is 7.0 mmol/kg body weight.[8]

In marasmus the ouabain – sensitive energy dependant sodium pump activity is decreased that causes raised intracellular sodium and decreased potassium. But children with kwashiorkor have increased leakiness of cell membrane by different mechanism.

The electrolyte abnormalities form the basis for recommendations to use low sodium in oral rehydration solutions (ORS), restriction of sodium and supplementation of potassium in every severe malnourished child. Hypophosphatemia also occur in undernourished children and is associated with high mortality. However, in India severe hypophosphatemia was not observed.

INTERACTION WITH INFECTION

Infection and nutrition are mutually interrelated in a vicious cycle that plays at several levels from cultural social interrelations to intracellular metabolism. Environmental factors are offers inadequate protein and energy intake are associated with conditions which bacterial and other microbial contamination is often rife.

Additionally poverty or famine, child's diet containing large amount of carbohydrate staples with little or no fat or animal products.

Animal products are milk, red meat, fish, egg, poultry are important bioavailable sources of micronutrients and minerals that have important role in fighting with infections.

Some metabolic changes occur during infection that focus on the boby energy resources to produce the acute phase proteins in the liver and are often opposite of those seen in starvation. The acute phase protein production and metabolic consequences of infection are mediated by lipid derived factors like leukotrienes, prostaglandins, protein cytokines, and platelet activation factor. Hormonal changes also play a role.

Catabolic hormones like glucagons, glucocorticoids, and epinephrine concentrations are increased. The cytokine interleukin (IL)-6 is rise the cortisol, glucagon, norepinephrine levels and important stimulus for mobilization of acute phase proteins in the liver.

The previous nutritional status of the child is altered the metabolic effect of infection. Children with marasmus have increased rate of breakdown and synthesis of structural protein in response to infection but not those with kwashiorkor and recovery from infective diarrhea also slow.

Cytokines and response to infection

Cytokines are produced by all nucleated cells, these are small, non structural proteins have both local and systemic effects involved in the

primary response to infection. Cytokine production is rapidly induced by infection, ischemia, trauma and other events. They are involved in changes in the protein metabolism and muscle function that accompany fasting, infection and cancer cachexia.

The proinflammatory cytokine mediators like IL-1, IL-6 involved in local inflammatory responses are redness, swelling, pain, local heat and systemic effects include fever and anorexia. The controlled mechanism of induction and synthesis of cytokine production are disturbed in malnutrition. Clinically severe malnourished children have blunted febrile response and reduced inflammatory reaction.[8]

Acute –Phase Proteins

Cytokine regulate the production of acute-phase proteins. The positive acute-phase proteins are alpha-1 antitrypsin, alpha-macroglobulin, C- reactive protein and fibronectin because their synthesis by liver increases in response to stress, like infection.

The negative acute-phase proteins are pre albumin, albumin, retinol binding protein, fibronectin are reduced in children with malnutrition. The positive acute-phase proteins play the important role in defence against infection but uncontrolled inflammation leads to adverse consequences like rheumatoid arthritis, inflammatory bowel disease and perhaps kwashiorkor.

Studies in Ghana on children without signs and symptoms of infection shows increased level of C-reactive protein in kwashiorkor and to lesser extent in marasmus. Alpha-1 acid glycoprotein level was raised in Thai children. The increase in serum levels of acute-phase proteins is attributable to reduction in catabolism rather than increase in protein synthesis in contrast to situation well nourished infected children.

In response to infection plasma fibrinogen normally increased, but no response in these children. The consequence of decreased inflammatory response to infection have important clinical repercussions because usual signs and symptoms of infection absent in malnutrition making diagnosis difficult and because mortality due to infection is greatly increased.

Free Radicals

Excess free radical production is basic explanation of the clinical findings in kwashiorkor. Free radicals produced by acute inflammatory cells during defense against infection with respiratory burst. This response to cell injury or infection depends on these free radicals for destruction of bacteria.

They are 1 or more unpaired electrons which cause them unstable or highly reactive. The reactive oxygen species are oxygen radicals like

singleton oxygen and nonradicals e.g hydrogen peroxide. The reactive nitrogen species are nitric oxide. Free radical production increased by infection, inflammation and environmental stresses.

Oxidative stress is a mechanism, normal balance between antioxidants and pro-oxidants is shifted toward oxidant side leads to increased free radical production which cause biologic damage. In kwashiorkor increased oxidative stress is demonstrated in studies. The free radicals cause damage to the nucleic acids, disrupting the enzymes and peroxidation of essential fatty acids and lipoproteins by hydrogen peroxide.

The enzymes neutralize the free radicals are glutathione peroxidase (selenium dependant), catalase and superoxide dismutase (zinc, copper dependant). Several studies showed concentrations of antioxidants is low in red cell and serum of the children with malnutrition, especially in kwashiorkor. The concentrations of vitamin E, glutathione and vitamin E to cholesterol ratio reduced in blood cells leads to diminished resistance to oxidative stress.

Polyunsaturated Fatty acids and Free Radicals

Essential fatty acids and their metabolites have protean functions like cell membrane integrity maintenance and immunologically active element synthesis such as leukotrienes and prostaglandins.[8] Antioxidant

levels are consistently reduced in protein energy malnutrition and this increases peroxidation of membrane long chain polyunsaturated fatty acids.

Arachidonic acid and glutathione are need for synthesis of leukotriens which is involved in inflammatory response. Several studies showed decreased level of whole blood glutathione and low urinary excretion in marasmus and kwashiorkor patients. It is due to leukotriene synthesis may be compromised in severe malnutrition.

Cysteine leukotrienes LTE4, LTC4 are involved in vascular damage and edema, these levels raised in RBCs of the kwashiorkor children but not marasmus, LTB4 level decreased which stimulate the chemotaxis.

In summary malnutrition seems as syndrome due to interplay of deprivation of nutrition and infectious or environmental stresses, which causes impaired balance in the normal physiologic response to these insults. This syndrome is predisposed by specific pattern of nutrient deficiencies include trace elements, proteins, sulfur amino acids, antioxidants.

CHANGES IN ORGANS AND SYSTEMS IN MALNUTRITION

Cardio vascular system

Cardiac output is reduced in acute protein energy malnutrition children when compared with recovery phase. Myocardial contractility is normal with nonspecific changes. Mild hypotension and sinus bradycardia may be present. Pericardial effusion is present in edematous malnutrition.

Associated deficiencies like anemia, hypokalemia and vitamin deficiencies affect the cardiac function. During recovery phase the heart size is increased due to the enlargement of cardiac chamber. The left ventricular muscle mass also increases proportionately to weight during the recovery period.

During rapid diet repletion sodium overload occur leading on to heart failure and sudden death. Adequate measures to be taken to restrict sodium intake include reducing the hyperalimentation and administration of diuretics to reverse the cardiac failure.

Animal studies have proved that malnutrition has direct effect on cardiovascular system. Alden et al did a study in dogs where a total of 21 dogs were selected for study. Among them regular diet was given to ten dogs and protein calorie deficient diet was given to eleven dogs to achieve mean weight loss of 20-25% over a three week period.

Echocardiographic evaluvation was done in both groups at one week (after the diet) and 3 weeks (after the diet). In the malnourished dogs, cardiac muscle mass was reduced in proportion to total body mass loss. The mean cardiac mass decreased from 115 to 91. This is mainly due to thinning of left ventricle wall. Heart rate decreased from 125 to 79 beats per minute, ejection fraction increased from 29.8 to 34.6%, cardiac output decreased from 2.98 to 2.38 liter per minute with malnutrition. But cardiac index normalized to body surface area was not changed. There was no significant hemodynamic change in the control group.

In cases global ventricular contractility as measured by the slope of linear relationship between end systolic pressure and end systolic volume or load independent index of systolic function slightly decreased from 3.56 to 2.81mmHg/ml. This indicates depressed contractility due to loss of cardiac muscle mass rather than any change in myocardium per se. During starvation the response to beta adrenergic stimulation was unchanged.

Acute protein energy malnutrition causes significant cardiac atrophy, reflected as reduced cardiac output and decreased contractility with no change in the intrinsic property of the myocardium.[26]

Ahmed H.Alanee did a study in malnourished children in Iraq. Accordingly mild malnutrition had a normal cardio-thoracic ratio and moderate to severe malnutrition had 20-40%. He also noted malnourished

children had significantly decreased left ventricular wall thickness in the posterior wall and septum, decreased ejection fraction, fractional shortening with decreased cardiac output and cardiac contractility.[27]

Heart muscle fibers were thinned out and the contractility of the myofibrils was impaired. Cardiac output, mainly systolic function, is decreased in the same proportion as the weight loss. Hypotension and bradycardia commonly occur in severe forms of malnutrition. Electrolyte imbalances occur during marasmus and are reflected as ECG findings. Along with this impaired cardiac function, any increase of intravascular volume like rehydration or blood transfusion can result in a significant cardiac insufficiency. The rapid electrolyte and metabolic energy changes in the initial phase of renutrition poses a higher risk for cardiac arrest and arrhythmia. Therefore, close clinical monitoring is crucial in children with circulatory compromise.[28]

Children with malnutrition are frequently associated with vitamins and micronutrient deficiencies. Among these thiamine and selenium are important with regard to the cardiovascular system.

Thiamine deficiency causes wet beriberi. Thiamine is an essential cofactor for carbohydrate metabolism. The amount of carbohydrate in the diet and physical exertion are essential contributing factors in the pathogenesis. Similarly infections particularly pneumonia associated with increased thiamine requirements may precipitate fulminant beriberi in

subclinical thiamine deficient individuals. Imapaired gastrointestinal absorption of thiamine due to chronic gastrointestinal disease is also a causative factor for beriberi.

Pathogenesis of cardiac beriberi includes dilatation and hypertrophy of both ventricles particularly right ventricle. Microscopically edema and hydropic degeneration occur especially in the conduction bundle and subendocardial muscle fiber along with marked edema of interstitial connective tissue. Mural thrombi are often attached with the trabeculae carneae of ventricles. No evidence of inflammation was seen.

The most common symptoms of cardiac beriberi are dyspnoea, swelling of ankles, non productive nocturnal cough and weakness. Examination of cardiovascular system reveals tachycardia, gallop rhythm and systolic murmur, less frequently soft diastolic murmur leads to diagnosis of aortic valve incompetency.

In severe disease patients are flushed, orthopenic, severely dyspneic and diffusely edematous due to heart failure. They may develop syncope or shock with sudden death. Specific therapy with thiamine could reverse these cardiovascular abnormalities and supportive therapy like oxygen, salt restriction, digitalis and diuretics may be needed in fulminant cases.[30, 31]

Selenium deficiency leads to cardiomyopathy called as Keshan disease. The acute form of this disease manifests as sudden onset of cardiac insufficiency, but chronic form results in moderate to severe cardiac enlargement with varying degrees of cardiac insufficiency. Selenium supplementation protects the people from developing Keshan disease, but cannot reverse cardiac muscle damage once it has occured.[32]

Severe protein energy malnutrition (PEM) presents in childhood as nonoedematous (marasmic) or oedematous (kwashiorkor) forms, with unknown long-term cardiovascular consequences. The cardiovascular function and structure will be poor in PEM survivors than unexposed controls.

Tennant IA et al, studied 116 adult PEM survivors, 62 after kwashiorkor, 54 marasmus. He selected 45 controls who werematched for age, sex and body mass index who had standardized echocardiography, blood pressure, anthropometry and arterial tonometry. Left ventricular indices and outflow tract diameter, pulse wave velocity, carotid parameters were measured and systemic vascular resistance calculated.

PEM survivors had mean reductions for pulse wave velocity, cardiac output, stroke volume and left ventricular outflow tract diameter when compared with controls but higher diastolic blood pressures. Systemic vascular resistance was higher in kwashiorkor and marasmus survivors than controls. No evidence of cardiac and large

vessel remodeling was found, except closer relationships between these indices in former marasmic survivors. Other parameters did not differ between PEM survivor groups.

They concluded that adult PEM survivors had smaller outflow tracts and cardiac output when compared with controls, but markedly elevated peripheral resistance. Finally malnutrition survivors are likely to develop excess hypertension in later life, especially when exposed to obesity.[29]

Respiratory system

In severe malnutrition the reduction of muscle mass affects the respiratory muscle function including the diaphragm which influences maximum inspiration and inspiratory pressures and vital capacity.

The electrolyte abnormalities like hypophosphatemia and hypokalemia may be exacerbate the weakness of the respiratory muscles. The blunted ventilator response to hypoxia is seen with no response to hypercapnia. Despite these alterations subcostal retraction and tachypnea are useful signs to diagnose pneumonia in children with malnutrition.

Gastrointestinal system

Malnutrition and diarrhea often occur together. Increased risk of prolonged diarrheal episodes are seen in malnutrition. High mortality occurs when malnutrition and persistent diarrhea (duration more than fourteen days) are concomitantly seen.

Both human and animal studies show severe malnutrition per se affect the gastrointestinal system leading to thinning of small intestinal mucosa, reduced gastric acid production, flattening or disappearance of villi with relative sparing of crypts.

The lamina propria layer shows increased cellularity seen in children with kwashiorkor. These structural changes causes altered mucosal function, increased permeability demonstrated by double sugar technique and malabsorption by nutrition absorption studies.

The loss of small intestinal villi architecture due to any cause decreases the disaccharidase activity, as lactase is mainly found in the villi tips. Thus lactose malabsorption is commonly seen in PEM.

Fat malabsorption is seen both in PEM and persistent diarrhea. Bacterial overgrowth in the upper GIT leads to bile salt deconjugation that further reduces the fat absorption.

Liver

The alteration of protein synthesis occurs in the liver. There is a shift from carrier protein synthesis to relative increase in acute inflammatory protein production which indicates the infection or injury response. These changes are markedly seen in kwashiorkor.

Liver enlargement is due to accumulation of triglycerides. During the recovery period these changes improve. There is no evidence that kwashiorkor per se leads to long-term hepatic damage like cirrhosis.

Endocrine system

Hormonal changes mediate the metabolic adaptation to starvation. Pancreatic atrophy is seen in malnutrition. In severe malnutrition decreased insulin level leads to diminished insulin response to glucagons, glucose load and arginine. This decreased insulin response increases the vulnerability of the child to any delay in starting feeds, so frequent small feeds are needed. Hypokalemia also contributes to these effects, so potassium supplements are important in malnutrition.

The insulin receptor affinity is also reduced in malnutrition. The endocrine effects rapidly reverse during refeeding leading to weight gain. Studies show increased concentration of growth hormone on admission but decreased serum levels during dietary treatment.

Serum cortisol level is increased mainly in kwashiorkor. The circadian rhythm is abolished but the response to adrenocorticotropic hormone is preserved. Increased level is associated with infection, 80% of the children showed raised cortisol level in kwashiorkor compared with only 50% of those with marasmus. This reduced response in children with marasmus explains their increased susceptibility to hypoglycemia.

The adrenaline hormone level is raised during initial period of hospitalization especially in kwashiorkor.

The function of thyroid gland is altered in malnutrition. During period of nutrition deprivation thyroxine (T4) level is increased but later in the more severe form in kwashiorkor total T4 level is decreased. Thyroid binding proteins are decreased and thyroid stimulating hormone levels are increased during recovery period. The T3 level is decreased due to reduction of deiodination of T4 to triiodothyronine (T3).

Immune system

Children with severe undernutrition are more susceptible to infections mainly associated with gram-negative organisms and death due to sepsis. There are marked alterations in complement system, cell mediated immunity, polymorphonuclear cell function and humoral immunity.

Cell-mediated Immunity

Cell-mediated immunity is impaired in severe malnutrition. Thymus gland is needed for normal differentiation of T cells is reduced in size with decreased thymic hormone production. Impairment of T cell function explained by decreased skin test response to recalled antigens e.g tuberculin test. The T4 cells are relatively reduced and T8 cells are only mildly affected. In gastrointestinal system gut-associated lymphoid aggregates are atrophied.

Humoral Immunity

Immunoglobulin production by B cells may be normal or raised. When administration of vaccine the seroconversion of immunoglobulin IgG is preserved. Although increased IgA has been reported, the response of secretory IgA in nasopharyngeal secretion after measles vaccination is reduced. In complement system C3 level is reduced and is related to protein metabolism. C4 level is increased or unaffected by nutritional status.

The phagocytic activity of polymorphonuclear cells is impaired in severe malnutrition. These alterations lead to decreased capacity of malnourished children to combat infection leading to increased risk of sepsis, which is one of the important reasons for mortality in severely malnourished children.

Hematology

Anemia is more common in severe malnutrition. These children are associated with iron deficiency anemia and decreased erythrocyte production in adaptation to smaller lean body mass. Most of the children consume low bioavailable iron in their diet.

During storage and transport iron is tightly bound to proteins to prevent free radical formation. In kwashiorkor decreased plasma transferrin, reflects reduced iron binding capacity hence free iron concentration may increase. Low plasma transferrin is related to increased mortality in hospitalized children with malnutrition. In children with kwashiorkor and those increased serum ferritin and high % of transferring saturation absorb less oral iron than those with decreased serum ferritin.

The iron problem is important as it plays a probable role in the etiology of kwashiorkor. Iron administration increases the mortality in acute protein energy malnutrition. Smith and colleagues conducted a study in Nigeria where 10 out of 31 children on iron supplementation at the time of admission had 3 deaths compare with 2 deaths out of the 12 children who did not receive any iron supplementation.

Iron is required during rehabilitation phase of increased lean body and red cell mass because iron stores are quickly exhausted so classic

features of iron deficiency occur. During this phase iron supplementation is necessary.

Serum folic acid levels is decreased. Folate supplementation corrects the megaloblastic changes in the bone marrow. Vitamin B2, vitamin E and copper deficiency are also seen in anemia with malnutrition.

Brain function and development

Most childhood malnutrition occurs during the period of rapid development, so any insult at this period leads to adverse consequences. The secondary effects on neural tissue in addition to the primary insult by anemia and micronutrient deficiencies cause apathy and reduced activity. Most undernourished children live in environment that fails to provide support and stimulation to the developing children to realize her or his potential.

After treatment, clinically recovered children return to this same environment, which makes it difficult to assess the impact of undernutrition per se on long term development. Studies done to compare the outcome of children (recovered from severe undernutrition) who either returned to home or adopted with families having more resources suggested that environmental influences outweighed the sequelae of undernutrition.

Skin, Hair and Teeth

In marasmus skin becomes dry, loose and wrinkled due to total loss of subcutaneous fat. It causes relative increase in surface area, reduced protection from environmental temperature and increased risk of hypothermia.

Hair becomes thin with slow growth and it easily falls out. On microscopy reduced hair root bulbs and shift to the resting state of hair growth was seen. Depigmentation is a classic sign and is called as hypochromotrichia. 'Flaky paint dermatosis' is pathognomonic in marasmus. The cracked lesions in buttock, groin and flexures can become infected and ulcerated to form crazy pavement dermatosis.

Skin changes in acrodermatitis enteropathica due to associated zinc deficiency improves with zinc ointments. The essential fatty acid deficiency, vitamin B complex and amino acid deficiencies also cause skin changes.

Even a single episode of prolonged malnutrition during the infancy period delays the primary dentition and is associated with a high prevalence of primary dentition caries and also permanent caries occur.

Bones

Children with severe acute malnutrition remain stunted even after recovery. Branca and colleagues described the cross linking of amino acids in collagen. Pyridinoline and deoxypyridinoline are excreted in urine in proportion to skeletal turnover. Their study shows skeletal turnover at lower rates insevere acute malnutrition and much higher levels during recovery.

Severity of wasting, age of the child on admission and cross link excretion accounted for 44 percent of the variability in height velocity during recovery. Bone demineralization is also seen due to phosphate deficiency.

Bone changes due to copper deficiency, scurvy due to vitamin C deficiency are also seen. Vitamin D deficiency causes osteomalacia and rickets. Vitamin D is necessary for B and T cell function mainly in phagocytosis. Children with rickets are more susceptible for pneumonia.

Recent studies show association between lower respiratory tract infection and low levels of serum 25-OH vitamin D3 in asymptomatic individuals. They are also more susceptible to tuberculosis mainly in those with vitamin D3 receptor polymorphisms. They are at more risk for chronic diseases like type 1 diabetes mellitus and certain malignancies in adults.

Children with malnutrition are more susceptible for vitamin deficiency due to decreased intake of calcium, inadequate vitamin D in breast milk, lack of dietary fat and reduced sun exposure as they stay indoors due to their illness.

CARDIAC TROPONINS

Cardiac troponins are a group of regulatory proteins involved in contractile process of myocardium of the heart. Three types of cardiac troponins are named as troponin C, troponin I and troponin T. They are situated in the actin filament at regular intervels.[25]

Cardiac specific troponin T and cardiac specific troponin I have different amino acid sequences compared to those present in skeletal muscle. These differences allow quantitative assay for cardiac troponin T and troponin I with highly specific monoclonal antibodies.[25]

Cardiac troponins are not normally detectable in healthy individual. They are twenty times more increased in myocardial infarction. These levels remain elevated for seven to ten days after myocardial infarction.[25]

Creatinine phosphokinase enzyme increaesed within four to eight hours after myocardial injury, but comes to normal within forty eight to seventy two hours. Creatinine kinase enzyme is often non specific as it may be elevated in skeletal muscle injury associated with intramuscular

injection. Hence cardiac troponins are now preferred as specific biochemical marker of myocardial injury.[25]

According to Newby et al, cardiac troponin T elevation is seen in non ischemic conditions like sepsis, heart failure, primary amyloidosis, chronic kidney disease and chemotherapy induced cardiomyopathy.[24]

Myocardial injury can occur in malnourished children with severe infection with sepsis. So cardiac specific troponin T is may be elevated in children with severe acute malnutrition.

REVIEW OF LITERATURE

Abu Faddan et al did echocardiographic evaluation in children with first degree, second degree, third degree marasmus, kwashiorkor and marasmic kwashiorkor. The left ventricle posterior wall diameter, interventricular septal diameter and left ventricle mass are significantly decreased in malnourished children compared with controls. These findings are more marked in third degree marasmus, kwashiorkor and marasmic kwashiorkor children.[9]

Also this study reviews parameters of left ventricle systolic function like ejection fraction and fractional shortening are significantly decreased in severely malnourished children than control group. But diastolic function (E/A ratio) is not significantly affected in cases compared with healthy controls.[9]

The cardiac troponin T level is increased, higher than upper reference value in children with severe acute malnutrition. Significantly increased cardiac troponin T level in children associated with sepsis, anemia and electrolyte deficiency.[9]

There is significant difference seen in biochemical parameters between cases and controls. The hemoglobin, serum total protein, albumin and serum calcium are significantly decreased in children with

malnutrition compared with controls. Total white blood cell count is significantly increased in cases than controls. But there is no significant changes seen in electrolytes like sodium and potassium between these two groups.[9]

HL El-Sayed et al noticed functional and structural changes in children with protein energy malnutrition on admission and after nutritional recovery. This study shows cardiac muscle mass was significantly reduced in both edematous and non edematous malnourished children compared with healthy controls, and after nutritional rehabilitation significant increased cardiac mass was seen in cases but less than healthy control group.[10]

This study showed left ventricle systolic function parameters ejection fraction and fractional shortening are not significantly decreased in children with protein energy malnutrition compared to healthy controls.[10]

There is no significant difference in E/A wave ratio, it reflects diastolic function of left ventricle is not significantly affected in malnourished children compared with control group. Two severely malnourished children had detection level of troponin I in their serum. [10]

They conclude systolic function is more affected than diastolic function especially in children with severe malnutrition, which indicate

bad prognosis. More intense management and strict follow up are necessary in those cases.

Serum albumin, hemoglobin are significantly decreased in malnourished children compared to control group and these parameters are significantly increased after nutritional rehabilitation. [10]

J W Bergman et al, echocardiographic evaluation done in only Kwashiorkor children, left ventricular end diastolic diameter, end systolic diameter, posterior wall diameter and interventricular septal thickness measured. The cardiac muscle mass is significantly reduced in severely malnourished children compared to age matched controls.[11]

This reduced muscle mass in the initial period of illness responsible for cardiomegaly and cardiac failure in later period during refeeding stage.[11]

Ocal et al, study on echocardiographic evaluation of severely malnourished children including marasmus, kwashiorkor and marasmic kwashiorkor. The left ventricular mass was decreased in proportion to reduced bodyweight in children with malnutrition. Left ventricular posterior wall diameter and septal thickness in children with protein energy malnutrition were decreased than controls.[12]

The left ventricular mass and posterior wall and septal thickness are significantly decreased in kwashiorkor children. Cardiac output decreased in proportion to reduced body size in malnourished children. There was no significant difference between cases and controls in cardiac index.[12]

The systolic parameters are fractional shortening and ejection fraction, diastolic function parameter E/A ratio were not significantly different between malnourished and healthy control groups.[12]

Olivares JL et al study described left ventricle mass and left ventricle mass index are significantly reduced in malnourished children. Serum calcium, potassium and albumin levels were decreased in children with malnutrition compared with control group.[13]

Special precaution must be taken in children with severe acute malnutrition because possibility of occurrence of sudden death and arrhythmias.[13]

They also noted elctrocardiographic changes such as corrected QT interval and QT dispersion were significantly greater in children with malnutrition than healthy controls.[13]

Singh GR et al, according to this study, children with grade III and grade IV protein energy malnourished children had significantly smaller ventricular wall thickness and cardiac chamber size compared to healthy normally nourished children.[14]

Cardiac output and other cardiac function indicators like ejection fraction, mean rate of circumferential fiber shortening and fractional shortening were significantly reduced in severe protein energy malnutrition.[14]

They also noted left ventricular dysfunction in moderate to severe protein energy malnourished children.[14]

Phornphatkul C et al described cardiovascular status of severe acute malnutrition before, during, after nutritional rehabilitation. Cardiac mass was reduced on admission to the hospital and recovered with nutritional therapy in majority of the children with third degree malnutrition.[15]

Echocardiogram and Doppler study shows ventricular dysfunction which was improved significantly during nutritional rehabilitation phase as evidenced by change in the mean velocity of circumferential fiber shortening, fractional shortening and systolic time interval.[15]

Special care should be taken with fluid therapy during the period of first week, because cardiac function more compromised in this period.[15]

Kothari SS et al, study showed, mean left ventricular mass was lower than healthy control children. The left ventricle systolic function parameters are fractional shortening, ejection fraction percentage and velocity of circumferential fiber shortening are not significantly different in malnourished children than healthy controls.[16]

Between marasmus and marasmic kwashiorkor children, there was no significant difference in indices of left ventricle function or mass. Reduced left ventricle mass indicates bad prognosis.[16]

P.M Smythe et al, noted malnourished child's heart is radiologically small due to wasting of muscle bulk, decreased overall diameter, both systolic and diastolic volume of the heart decreased related to decreased blood volume and venous return. Myocardial atrophy is evidenced by subnormal heart weight was detected during autopsy.[17]

They also found very thin right ventricle, thinness of the ventricular wall, decreased heart weight, flabbiness of the heart muscle in autopsy of suddenly died kwashiorkor child.[17]

According to **ver Elst KM et al,** clinically unrecognized cardiomyocyte injury is a marker of left ventricle dysfunction in patients with septic shock. The cardiac troponin T and troponin I were significantly increased patients have worse survival rate. The left ventricle function was assessed by two dimensional transesophageal echocardiography.[18]

Ammann P et al, described cardiomyocyte injury occurs in severe systemic inflammation which is proved by raised cardiac troponin I in sepsis and septic shock patients without acute coronary syndrome.[19]

Cardiac troponin I significantly increased in patients with sepsis, septic shock and systemic inflammatory response syndrome.[19]

checchia et al described myocardial damage seen in children with documented respiratory syncytial virus infection as evidenced by increased cardiac troponin I level in their serum.[20]

Khan IA et al noted cardiac troponin I level was increased in non cardiac and cardiac diseases like chronic renal failure, HIV disease, muscular disorders, non ischemic dilated cardiomyopathy, central nervous system disorders, endocrine disorders and lung diseases.[21]

They also described cautious interpretation of lower range cardiac troponin I level, especially during acute illnesses, lack of other diagnostic symptoms and signs suggestive of acute coronary ischemic events.[21]

Maggiorini et al, noted increased troponin level is risk factor for mortality in intensive care patients admitted for reason other than acute coronary syndrome. It is also associated with reduced left ventricular function and increased levels of tumour necrosis factor alfa and interleukin -6.[22]

Gunnewiek JM et al described increased troponin levels are not only in acute coronary syndrome patients, also present in critically ill patients. Even mild increased level of troponin is specific for myocardial injury.[23]

AIM OF THE STUDY

To compare the cardiac muscle mass and cardiomyocyte injury in children with severe acute malnutrition with age, sex matched controls.

STUDY JUSTIFICATION

According to world health organization, worldwide nearly 20 million children are affected by severe acute malnutrition, among them most of the children living in sub-Saharan Africa and South Asia.

Malnutrition is a major public health and developmental issue in developing countries like India as well as other parts of the world in the under five age group of children.

Currently 1million children die due to severe acute malnutrition in every year. This mortality rate is 5-20 times higher compared to well nourished children.

According to Indian Academy of Pediatrics, Severe acute malnutrition estimated to be 8.1 million under-five children in India causing nearly 0.6 million deaths.

Children with severe acute malnutrition suffered from many changes in body composition with loss of skeletal and cardiac muscle mass, which is complicated by vitamin and mineral deficiencies and electrolyte abnormalities that can produce cardiac abnormalities, including cardiac arrhythmias, hypotension, cardiomyopathy, heart failure and even sudden death.

Cardiac troponin T is highly sensitive and specific biomarker of cardimyocyte injury and cardiac troponin T positive malnourished

children have high mortality reported compared to troponin negative malnourished children.

The outcome of this study may help about the importance of adequate nutrition intake among under five children and reduces morbidity and mortality in severe acute malnourished children.

MATERIALS AND METHODS

METHODOLOGY

STUDY PLACE : Institute of Child Health and Hospital for Children, Madras Medical College, Egmore, Chennai.

STUDY DESIGN : Case control study.

STUDY PERIOD : April 2014 to November 2014

STUDY POPULATION: According to World Health Organization children with severe acute malnutrition are included in this study severe malnourished children are included in this study.

CONFLICT OF INTEREST : Nil

FINANCIAL SUPPORT : Nil

ETHICAL COMMITTEE CLEARANCE **:** Obtained

SAMPLE SIZE **:** 41 cases and 21 controls

INCLUSION CRITERIA

Cases included according to WHO diagnostic criteria for children with severe acute malnutrition aged 6 months to 5yrs.

Severe wasting	MUAC	<115 mm
Severe wasting	Weight -for- Height	<-3 SD
Bilateral edema	Clinical sign	

EXCLUSION CRITERIA

- Pre-term or intrauterine growth retardation at birth.
- Congenital and acquired heart disease
- Severe anemia (<7gm/dl)

MANOEUVRE

This study was conducted in at tertiary care hospital in tamilnadu which receives the cases not only from tamilnadu but also from the nearby states. Children with severe acute malnutrition who fulfilled the inclusion criteria were included in the study, the children were recruited

from nutrition outpatient department as well as children who were admitted in the pediatric medical ward.

Children were included in this study only after obtaining informed consent from parents or guardian. Weight, height, mid upper arm circumference were measured echocardiographic evaluation for cardiac dimension and wall thickness, estimation of indices of left ventricle systolic and diastolic function and cardiac troponin level estimation was done for the children.

The children were weighed using electronic weighing scale with little clothing as per customs allowed and without any contact with other object.

Below 2 yrs of age length was measured by using infantometer or measuring rod ideally by two persons.

The child was placed on the infantometer, head fixed to the vertical head board while child's eyes are looking upwards. The other person was press the knees together and directed downwards, so back of knees touches horizontal surface of infantometer. Then foot end of the board is adjusted by moving towards the heel of the child. The accuracy of length measurement was adjusted to nearest 0.5 cm.

Above 2 yrs of age height was measured by using stadiometer or vertical measuring rod. The child was allow to stand with bare foot and occiput, shoulders, buttocks and heels are touching the wall and looking

straight in Frankfurt plane. The observer took the measurement after lowering the cursor or placing a book or wooden board horizontally on the top of the head with touching the hair. The accuracy of the height measurement was nearest to 0.5 cm.

Weight and length or height was measured by the above methods. World health organization nutritional growth chart was used to grade the anthropometry. According to this chart, weight for length or weight for height z score less than -3 standard deviation are classified as severe acute malnutrition and were included in this study. The weight for length/ height z score is between -2 to -3 standard deviation are classified as moderate acute malnutrition excluded from this study.

Mid upper arm circumference measured by placing the arm touching with body surface, locate the tip of the shoulder and elbow, place the tape from tip of the shoulder to tip of the elbow with the forearm in flexed position, the mid point of this measurement was taken as the mid upper arm circumference. Mid upper arm circumference was measured in children with age one to five years. children with mid upper arm circumference less than 11.5 cm are classified as severe acute malnutrition included in this study as cases.

According to world health organization growth chart, children with weight for length or weight for height z score between -1 to +3 standard deviation were considered as normal and were included as control.

Between one and five years of age, mid upper arm circumference is more than 12.5 cm were recruited as control group in this study. Echocardiographic evaluvation was done in all the children included in the study. Echocardiography is extremely safe, useful, noninvasive test used for diagnosis and management for heart disease. Echocardiographic studies useful for anatomic as well as functional diagnosis. The M mode echocardiography provides “ice-pick” view of the heart. It is used for measurement of cardiac chamber dimensions as well as timing. Doppler study and color mapping are used to detect valve regurgitation and cardiac shunt lesions during echocardiographic examination.

In echocardiography M mode obtained by placing the ultrasonic transducer along left sternum border directed toward the cardiac part to be examined. Left ventricle posterior wall diameter, interventricular septal thickness, left ventricular chamber dimensions during diastole and systole are measured.

Left ventricle mass and left ventricle mass index are calculated by LVMI calculator with left ventricle end diastolic diameter, posterior wall diameter interventricular septal diameter parameters indexed to body surface area (g/m^2).

Normal left ventricular mass index

Male - 49 -115 g/m^2

Female - 43 – 95 g/m^2

Left ventricular systolic function evaluated by ejection fraction, fractional shortening and systolic time interval.

Fractional shortening is reliable and reproducible index of left ventricular function, provided there is no abnormal regional wall motion and there was concentric contractility of left ventricle. If interventricular septal movement is paradoxical or flat, fractional shortening will not accurately calculate the ventricular ejection.

Fractional shortening is calculated by using following formula.

FS (%) = LVEDD – LVESD / LVEDD ×100

Normal fractional shortening : 36 % (28 – 44)

FS - Fractional shortening

LVEDD - Left ventricle end diastolic diameter

LVESD - Left ventricle end systolic diameter

Ejection fraction is derived from fractional shortening and it gives no advantage over shortening fraction. It is related to change in the volume of left ventricle with cardiac contraction. Ejection fraction is calculated by using following formula.

EF (%) = $LVEDD^2$-$LVESD^2$/$LVEDD^2$ ×1OO

Normal ejection fraction: 66 % (56 – 78)

EF - Ejection fraction

LVEDD - Left ventricle end diastolic diameter

LVESD - Left ventricle end systolic diameter

Left ventricle diastolic function assessed by blood flow across the mitral valve during early diastolic filling (E wave) of left ventricle and atrial contraction (A wave) measured by Doppler echocardiography. When diastolic dysfunction suspected by LAOT

Normal E/A Ratio : 2 (1.5 - 2.5)

Two milliliter of blood were collected from both cases and control by venepuncture after proper cleaning with povidone iodine antiseptic solution and alcohol. After sample collection the blood was allowed to clot then centrifugation was done to separate the serum. Cardiac troponin T level is measured by using electrochemiluminescence immunoassay (ECLIA) method. Interpretation of serum troponin level was below 0.01 nanogram per milliliter was considered as normal, 0.01 to 0.09 nanogram per milliliter indicates borderline elevation and more than 0.10 nanogram per milliliter indicates myocardial injury. All informations were recorded in the data collection sheet.

Healthy controls were recruited from the children who attend the immunization outpatient department for vaccination.

STATISTICAL ANALYSIS

All data collected are by data collection form then entered in excel spread sheet. For statistical analysis SPSS version 16 is used. The standard deviation and mean are calculated for continuous data. To compare the mean echocardiography variables and cardiac Troponin T level between two groups Independent t test is used.

RESULTS

The study population consists of 62 children with 41 cases and 21 controls.

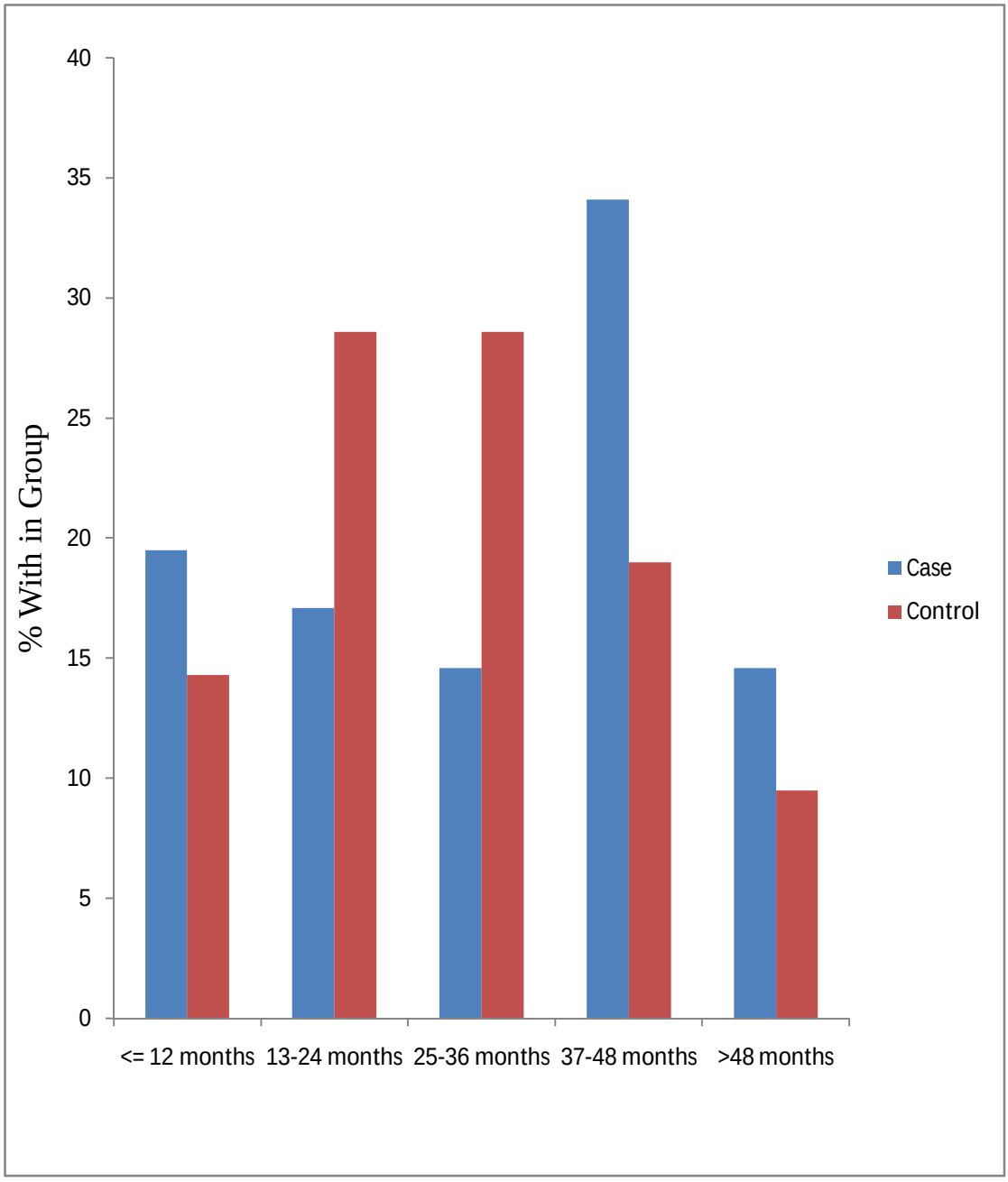
AGE DISTRIBUTION

The age distribution in cases are eight children less than or equal to twelve months of age. Seven children are between thirteen to twenty four months. Six children are between twenty five months to thirty six months. Fourteen children are thirty seven months to forty eight months. Six children are more than forty eight months.

In control group three children are less than or equal to twelve months of age. Six children are between thirteen to twenty four months. Six children are between twenty five months to thirty six months. Four children are thirty seven months to forty eight months. Two children are more than forty eight months.

			Group		Total
			Control	Cases	
Age in months	<= 12	Count	3	8	11
		% within Age in months	27.3%	72.7%	100.0%
		% within Group	14.3%	19.5%	17.7%
	13-24	Count	6	7	13
		% within Age in months	46.2%	53.8%	100.0%
		% within Group	28.6%	17.1%	21.0%
	25-36	Count	6	6	12
		% within Age in months	50.0%	50.0%	100.0%
		% within Group	28.6%	14.6%	19.4%
	37-48	Count	4	14	18
		% within Age in months	22.2%	77.8%	100.0%
		% within Group	19.0%	34.1%	29.0%
	> 48	Count	2	6	8
		% within Age in months	25.0%	75.0%	100.0%
		% within Group	9.5%	14.6%	12.9%
Total		**Count**	**21**	**41**	**62**
		% within Age in months	**33.9%**	**66.1%**	**100.0%**
		% within Group	**100.0%**	**100.0%**	**100.0%**

Table: 1. Age Distribution



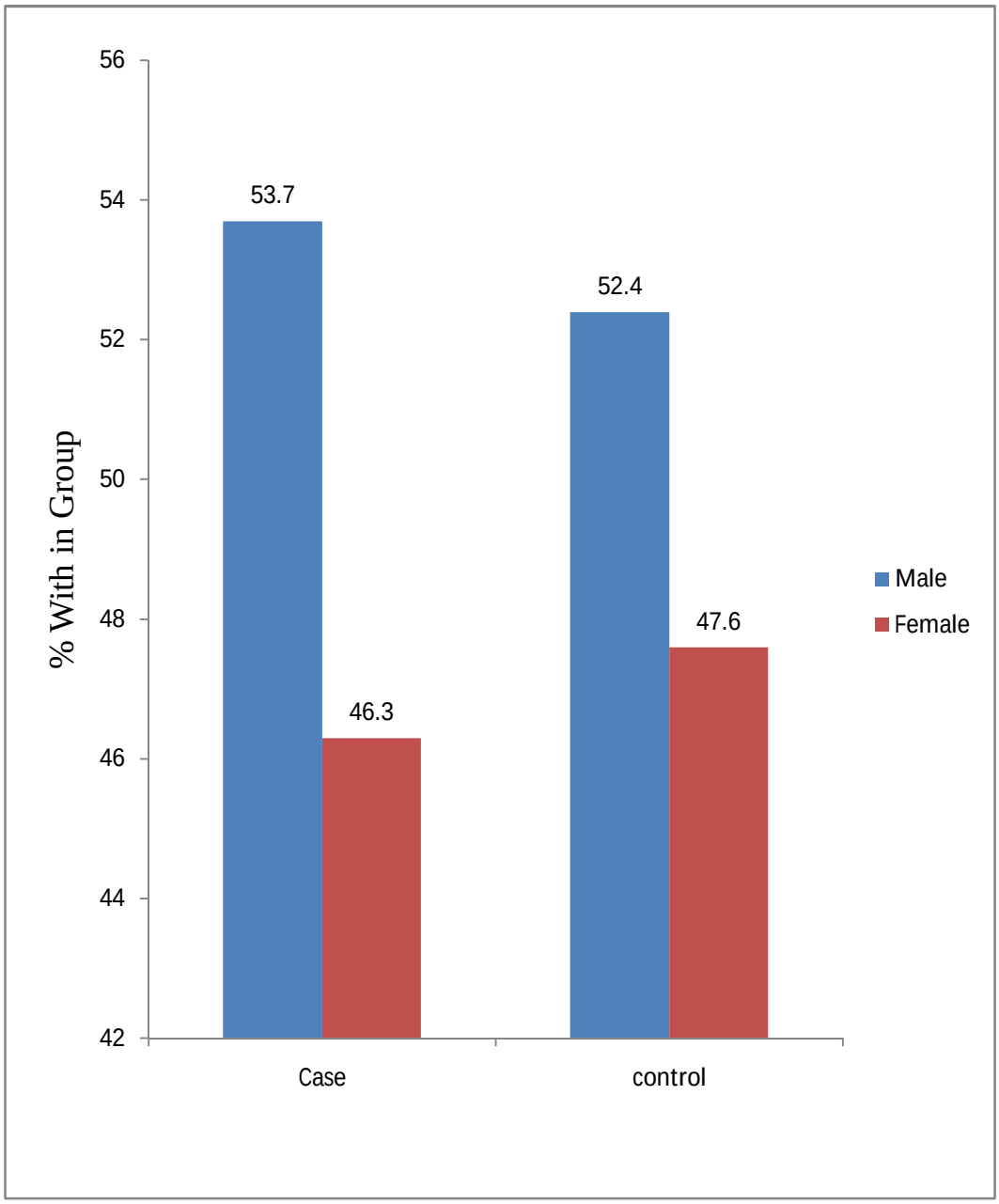
AGE DISTRIBUTION

SEX DISTRIBUTION

Totally forty one severely acute malnourished children are recruited, there are twenty two male children, nineteen female children. Totally twenty one healthy children recruited as control among these eleven male children and ten female children.

Sex		Group		Total	P value
		Controls	Cases		
Male	Count	11	22	33	0.924
	% within sex	33.3 %	66.7 %	100.0 %	
	% within group	52.4 %	53.7 %	53.2 %	
Female	Count	10	19	20	
	% within sex	34.5 %	65.5 %	100.0 %	
	% within group	47.6 %	46.3 %	46.8 %	
Total	Count	21	41	62	
	% within sex	33.9 %	66.1 %	100.0 %	

Table: 2 Sex distribution



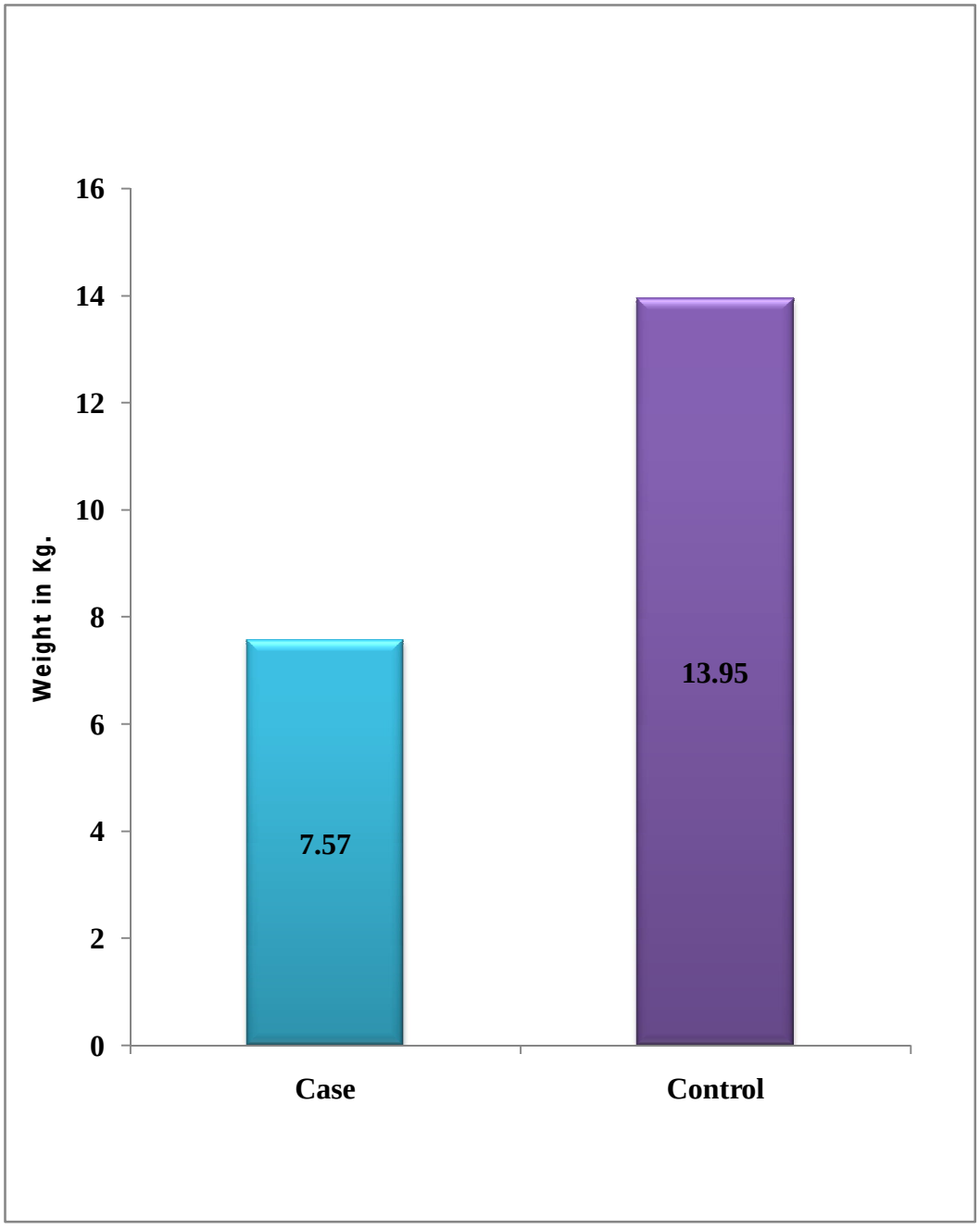
SEX DISTRIBUTION

WEIGHT

Mean weight in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in the weight. Mean weight of the children with severe acute malnutrition is 7.570 kilogram. The mean weight of the children in control group is 13.952 kilogram. Mean weight of the children with severe acute malnutrition is significantly lower than their matched controls ($p<0.001$).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
Weight (kg)	Control	21	13.952	3.0730	<0.001
	Case	41	7.570	1.4903	

Table: 3 Weight in case and control



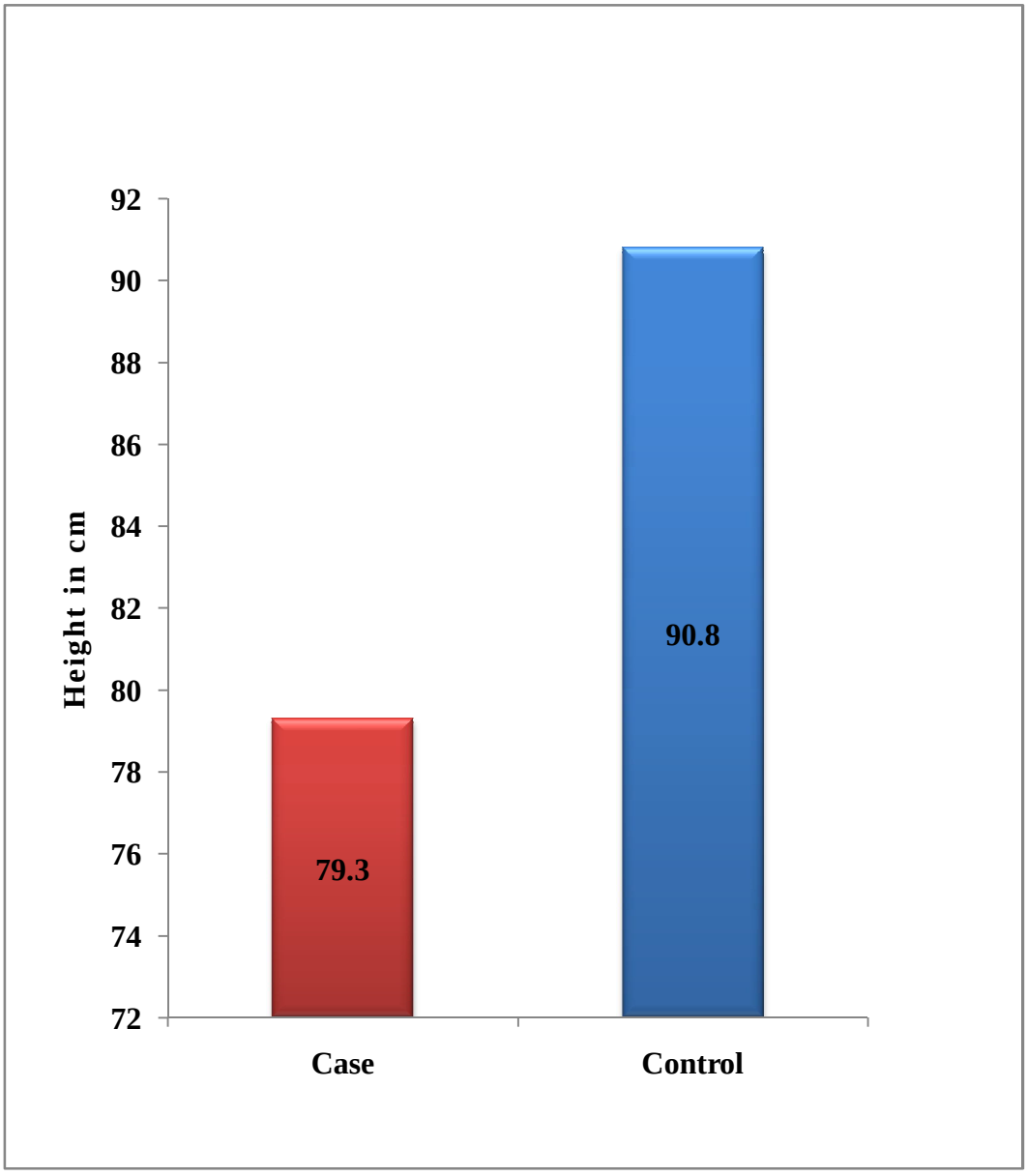
COMPARISON OF WEIGHT BETWEEN CASE AND CONTROL

HEIGHT

Mean height in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in the height. Mean height of the children with severe acute malnutrition is 79.342 centimeter. The mean height of the children in control group is 90.857 centimeter. Mean height of the children with severe acute malnutrition is significantly lower than their matched controls ($p<0.001$).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
Height(cm)	Control	21	90.857	11.0873	<0.001
	Case	41	79.341	8.4930	

Table: 4 Height in case and control



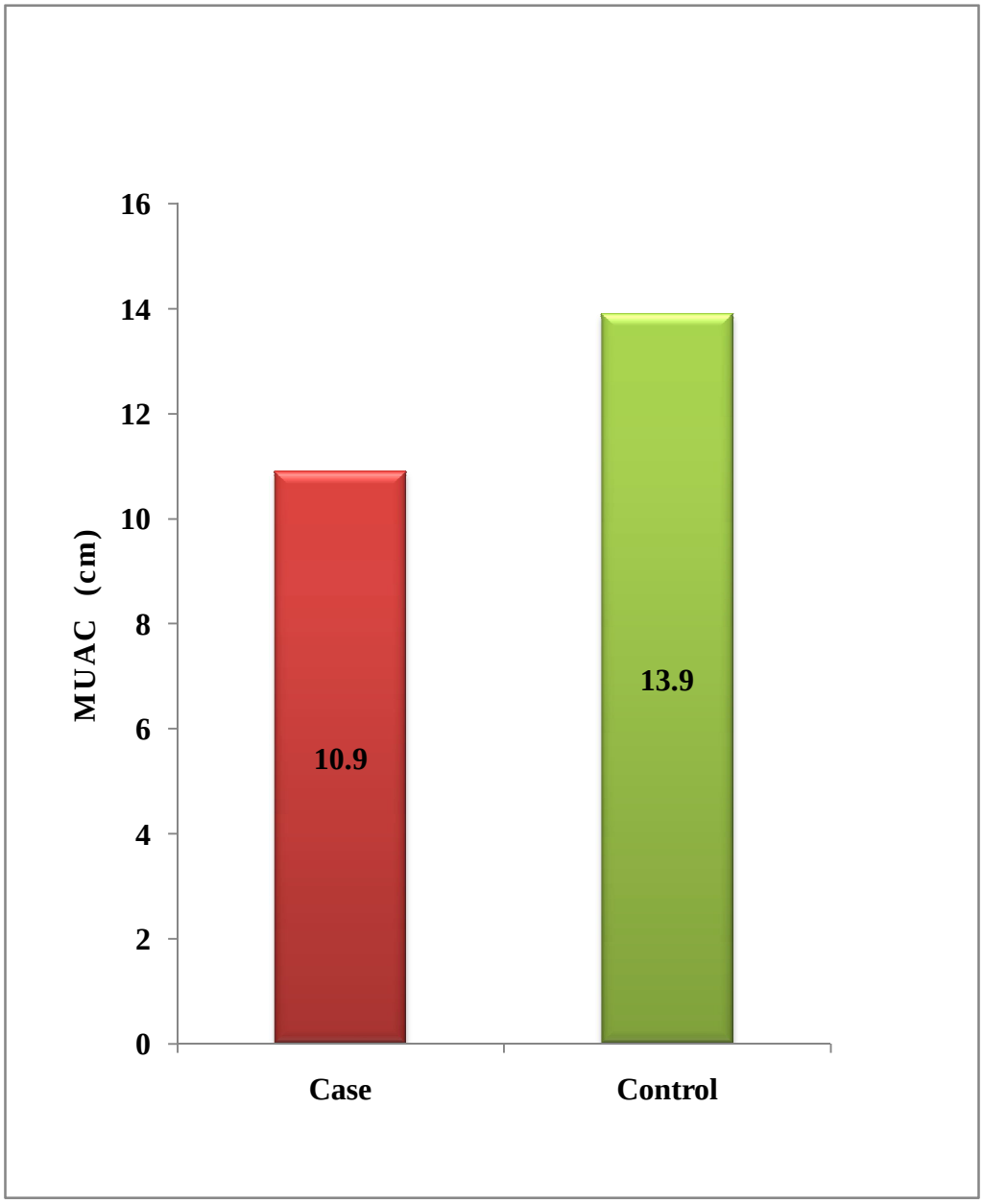
COMPARISON OF HEIGHT BETWEEN CASE AND CONTROL

MID UPPER ARM CIRCUMFERENCE

Mean mid upper arm circumference in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in the mid upper arm circumference. Mean mid upper arm circumference of the children with severe acute malnutrition is 10.928 centimeter. The mean mid upper arm circumference of the children in control group is 13.900 centimeter. Mean mid upper arm circumference of the children with severe acute malnutrition is significantly lower than their matched controls ($p<0.001$).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
MUAC (cm)	Control	19	13.900	0.4643	< 0.001
	Case	39	10.928	0.4205	

Table: 5 Mid Upper Arm Circumference in case and control



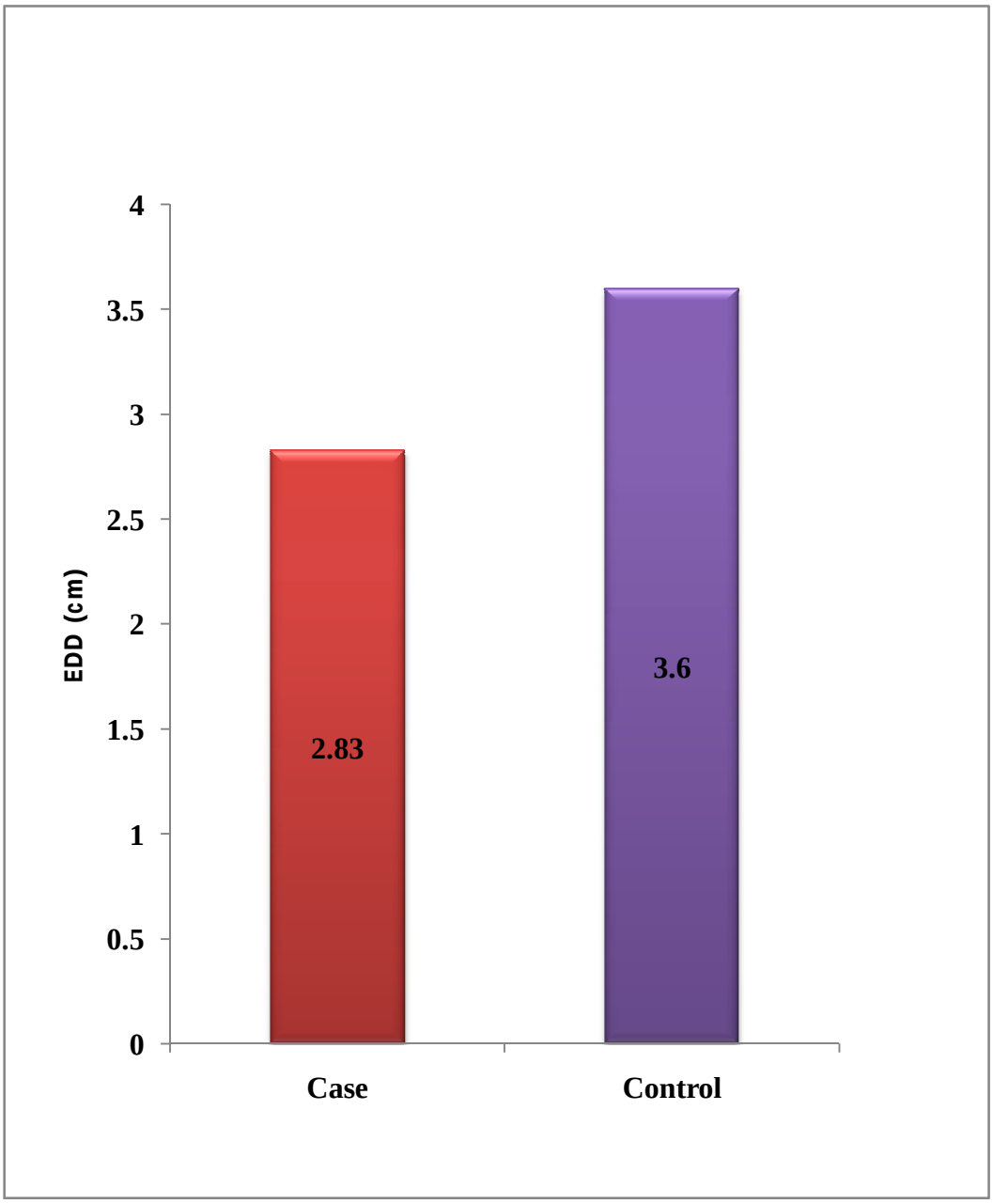
COMPARISON OF MID UPPER ARM CIRCUMFERENCE BETWEEN CASE AND CONTROL

LEFT VENTRICLE-END DIASTOLIC DIAMETER

Mean left ventricle end diastolic diameter in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in left ventricle end diastolic diameter. Mean left ventricle end diastolic diameter of the children with severe acute malnutrition is 2.8388 centimeter. The mean left ventricle end diastolic diameter of the children in control group is 3.6057 centimeter. Mean left ventricle end diastolic diameter of the children with severe acute malnutrition is significantly lower than their matched controls ($p<0.001$).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
EDD (cm)	Control	21	3.6057	0.30091	< 0.001
	Case	41	2.8388	0.43143	

Table: 6 Left ventricle end diastolic diameter in case and control



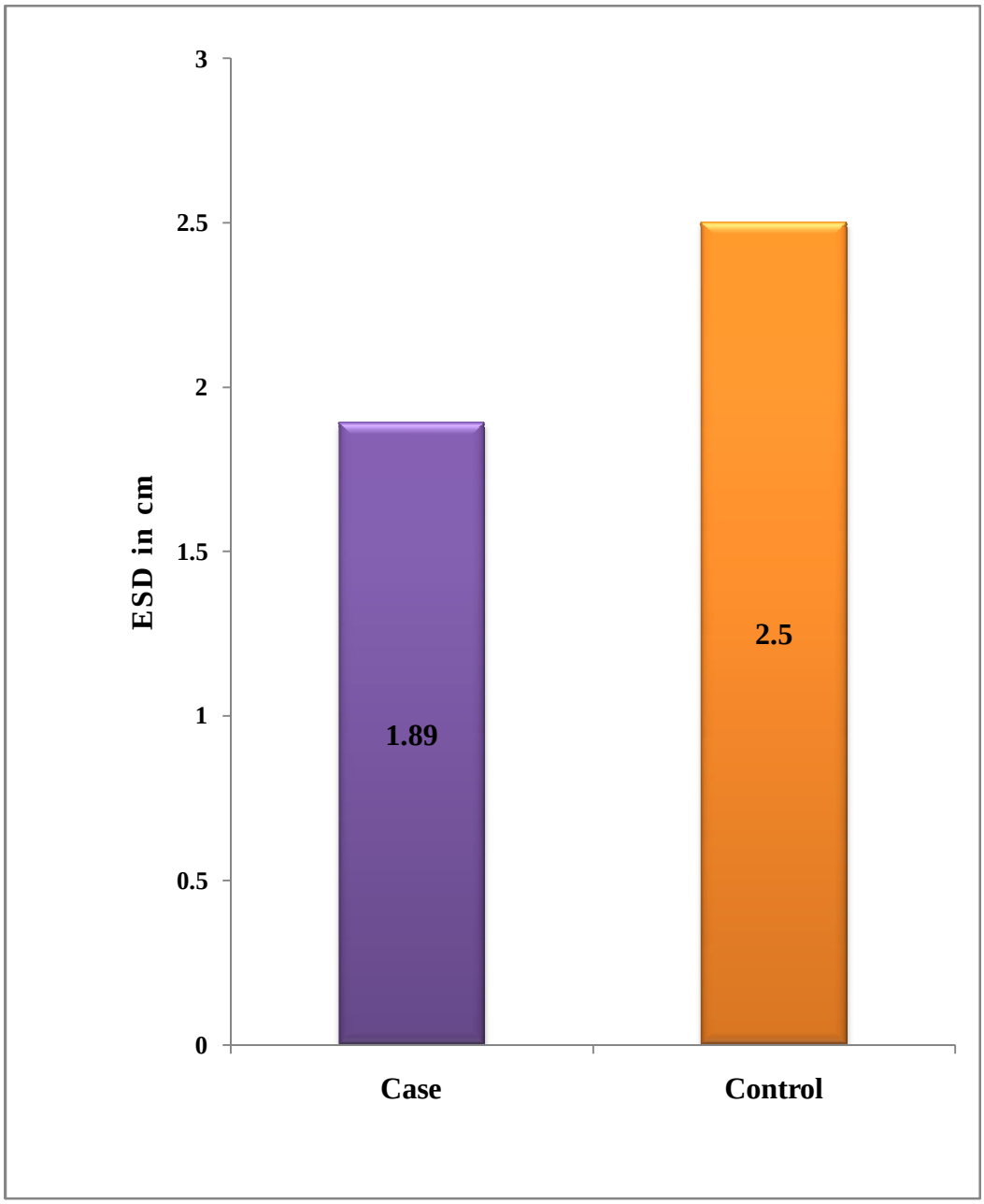
COMPARISON OF LEFT VENTRICLE-END DIASTOLIC DIAMETER BETWEEN CASE AND CONTROL

LEFT VENTRICLE-END SYSTOLIC DIAMETER

Mean left ventricle end systolic diameter in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in left ventricle end systolic diameter. Mean left ventricle end systolic diameter of the children with severe acute malnutrition is 1.8978 centimeter. The mean left ventricle end systolic diameter of the children in control group is 2.3933 centimeter. Mean left ventricle end systolic diameter of the children with severe acute malnutrition is significantly lower than their matched controls ($p<0.001$).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
ESD (cm)	Control	21	2.3933	0.18866	< 0.001
	Case	41	1.8978	0.34157	

Table: 7 Left ventricle end systolic diameter in case and control



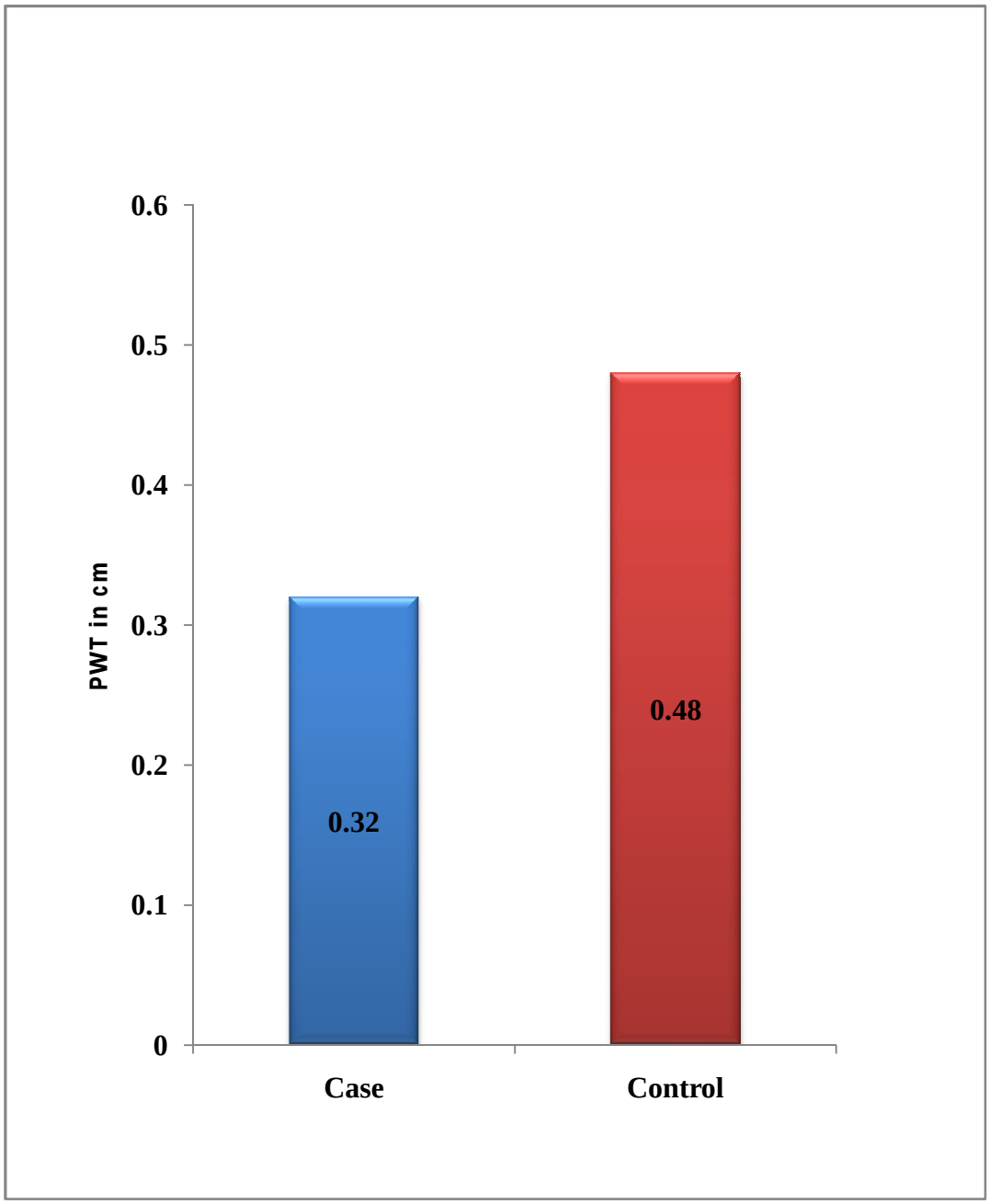
COMPARISON OF LEFT VENTRICLE-END SYSTOLIC DIAMETER BETWEEN CASE AND CONTROL

LEFT VENTRICLE – POSTERIOR WALL THICKNESS

Mean left ventricle posterior wall thickness in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in left ventricle posterior wall thickness. The Mean left ventricle posterior wall thickness of the children with severe acute malnutrition is 0.3276 centimeter. The mean left ventricle posterior wall thickness of the children in control group is 0.4857 centimeter. Mean left ventricle posterior wall thickness of the children with severe acute malnutrition is significantly lower than their matched controls ($p<0.001$).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
PWT (cm)	Control	21	0.4857	0.06918	< 0.001
	Case	41	0.3276	0.04999	

Table: 8 Left ventricle posterior wall diameter in case and control



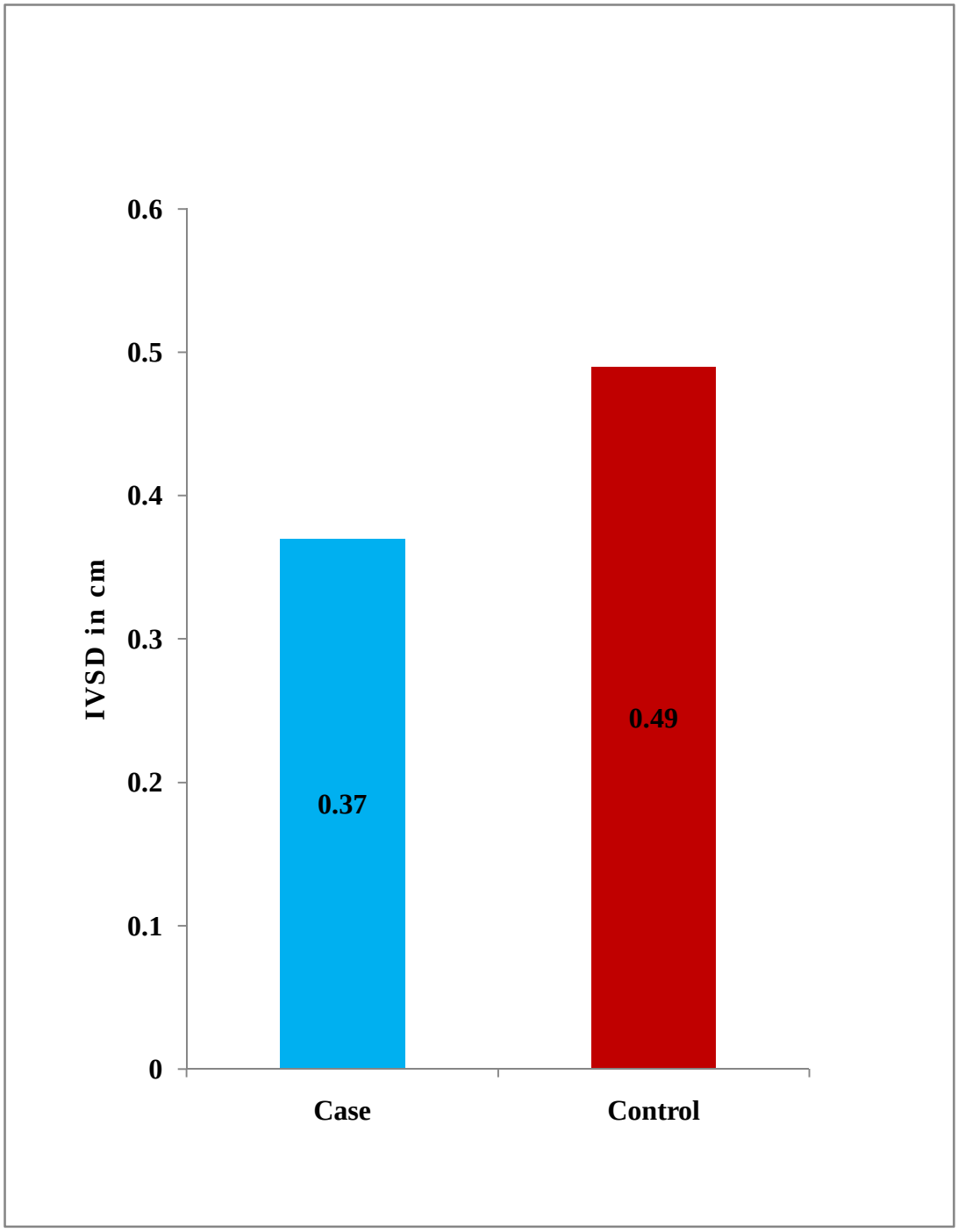
COMPARISON OF LEFT VENTRICLE – POSTERIOR WALL THICKNESS BETWEEN CASE AND CONTROL

INTER-VENTRICULAR SEPTAL THICKNESS

Mean inter-ventricular septal thickness in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in inter-ventricular septal thickness. Mean inter-ventricular septal thickness of the children with severe acute malnutrition is 0.3726 centimeter. The mean inter-ventricular septal thickness of the children in control group is 0.4929 centimeter. Mean inter-ventricular septal thickness of the children with severe acute malnutrition is significantly lower than their matched controls ($p<0.001$).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
IVSD (cm)	Control	21	0.4929	0.06619	< 0.001
	Case	41	0.3737	0.07081	

Table: 9 Inter-ventricular septal thickness in case and control



COMPARISON OF INTER-VENTRICULAR SEPTAL THICKNESS BETWEEN CASE AND CONTROL

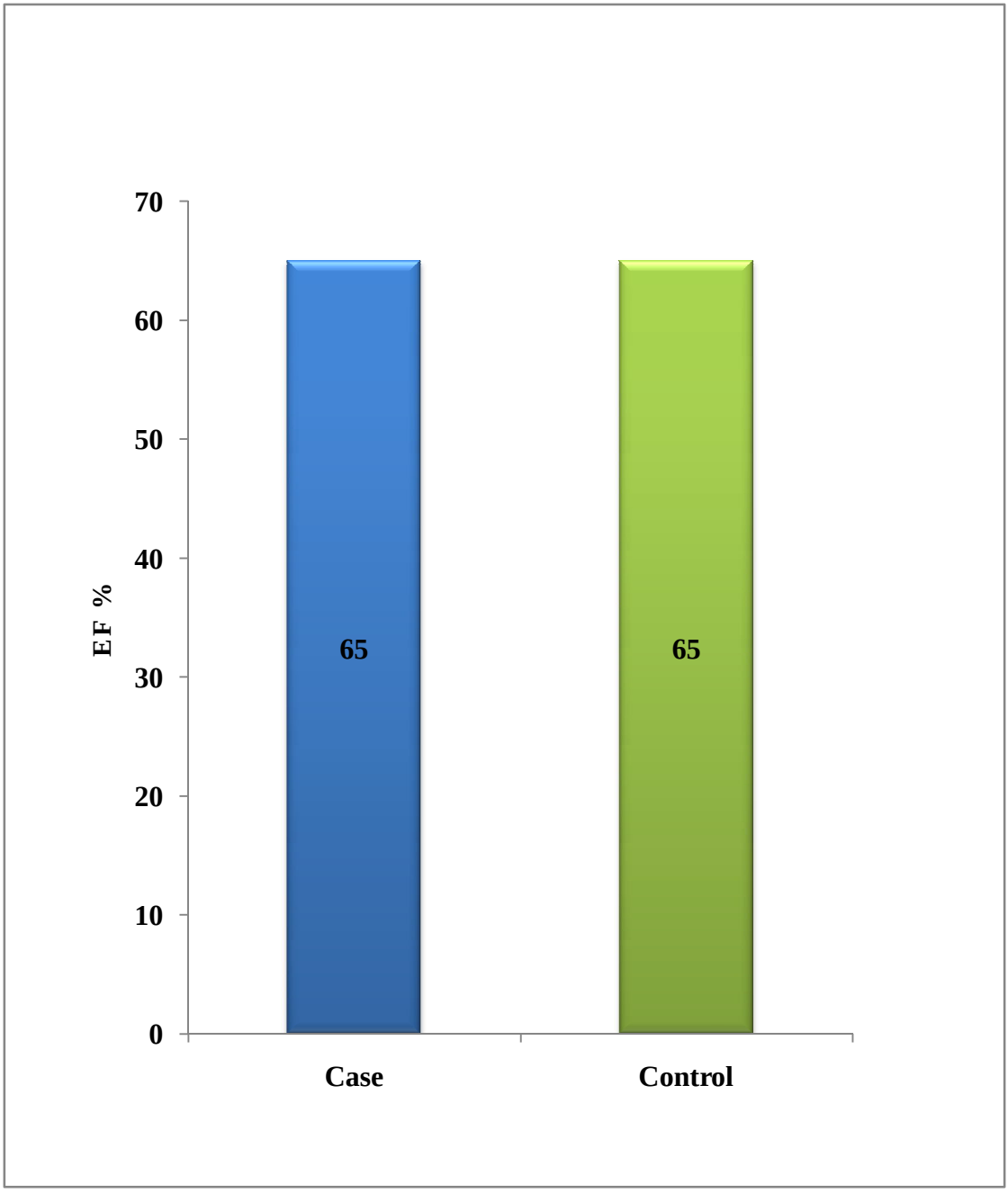
LEFT VENTRICLE-EJECTION FRACTION

Mean left ventricle ejection fraction in children with severe acute malnutrition is compared with their control group. There is no significant difference between children with severe acute malnutrition and controls in the left ventricle ejection fraction. Mean left ventricle ejection fraction of the children with severe acute malnutrition is 65.024 percent. The mean left ventricle ejection fraction of the children in control group is 65.895 percent. Mean left ventricle ejection fraction of the children with severe acute malnutrition is not significantly lower than their matched controls (p=0.404).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
EF (%)	Control	21	65.895	1.4313	0.404
	Case	41	65.024	4.6149	

Table: 10 Left ventricle ejection fraction in case and control

EF – Ejection fraction



COMPARISON OF LEFT VENTRICLE-EJECTION FRACTION BETWEEN CASE AND CONTROL

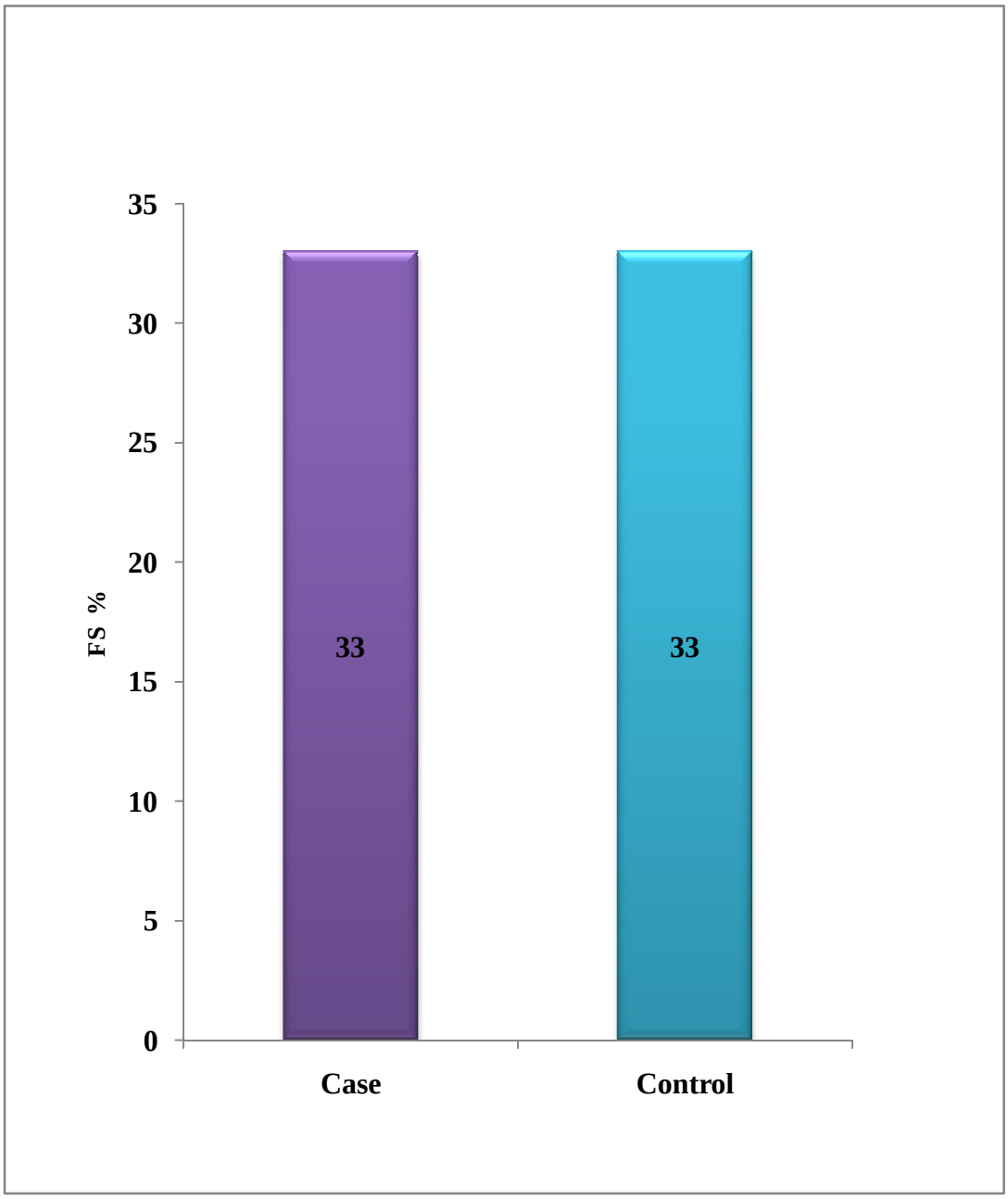
LEFT VENTRICLE – FRACTIONAL SHORTENING

Mean left ventricle fractional shortening in children with severe acute malnutrition is compared with their control group. There is no significant difference between children with severe acute malnutrition and controls in the left ventricle fractional shortening. Mean left ventricle fractional shortening of the children with severe acute malnutrition is 33.354 percent. The mean left ventricle fractional shortening of the children in control group is 33.548 percent. Mean left ventricle fractional shortening of the children with severe acute malnutrition is not significantly lower than their matched controls (p=0.809).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
FS (%)	Control	21	33.548	1.1609	0.809
	Case	41	33.354	3.5470	

Table: 11 Left ventricle fractional shortening in case and control

FS-Fractional shortening



COMPARISON OF LEFT VENTRICLE FRACTIONAL SHORTENING BETWEEN CASE AND CONTROL

MITRAL VALVE – E/A RATIO

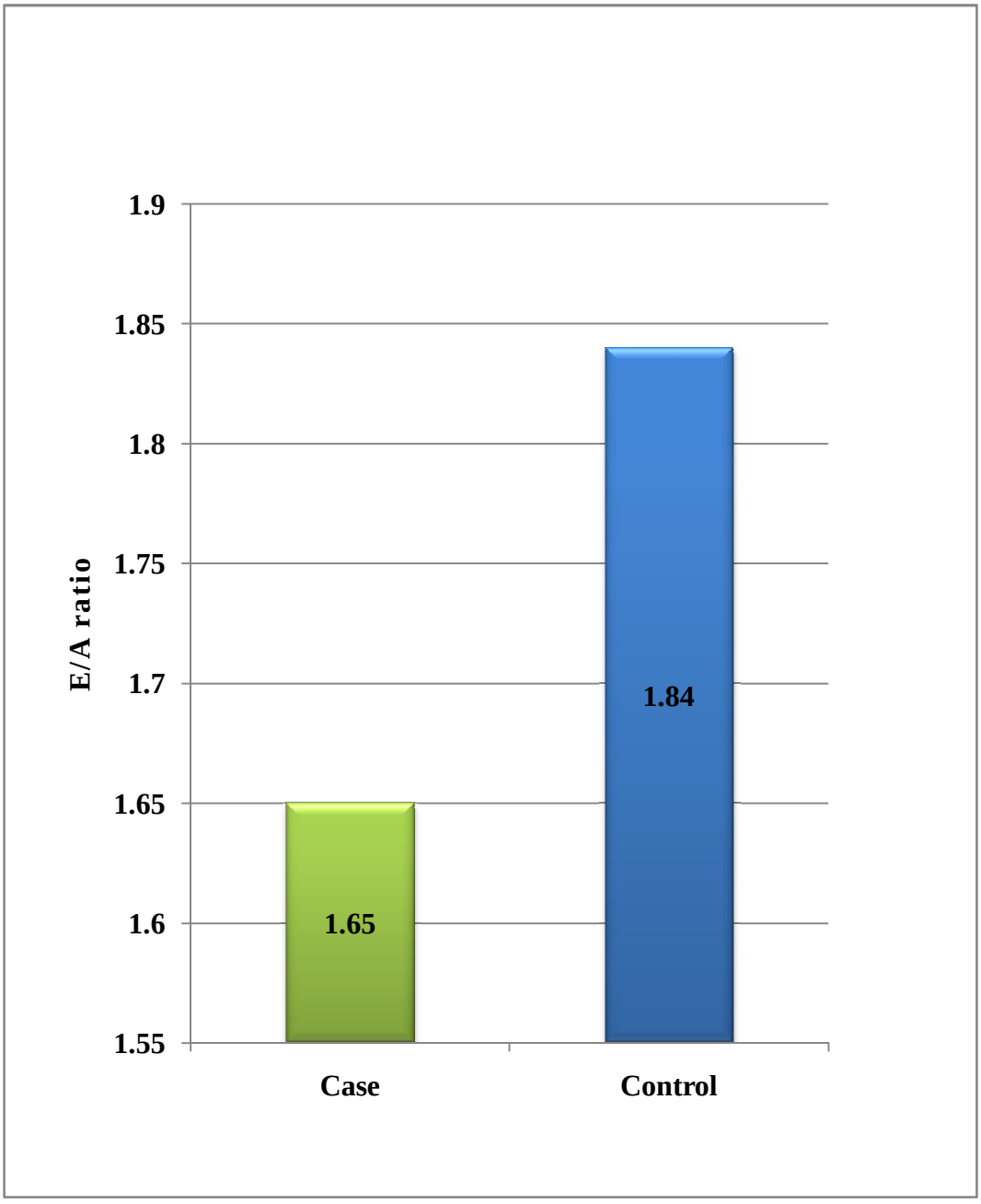
Mean mitral valve E/A ratio in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in mitral valve E/A ratio. Mean mitral valve E/A ratio of the children with severe acute malnutrition is 1.655. The mean mitral valve E/A ratio of the children in control group is 1.846. Mean mitral valve E/A ratio of the children with severe acute malnutrition is significantly lower than their matched controls (P value= 0.008).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
E/A Ratio	Control	21	1.846	0.2823	0.008
	Case	41	1.655	0.2455	

Table: 12 E/A ratio in case and control

E wave - wave during early diastolic filling

A wave - wave during atrial contraction



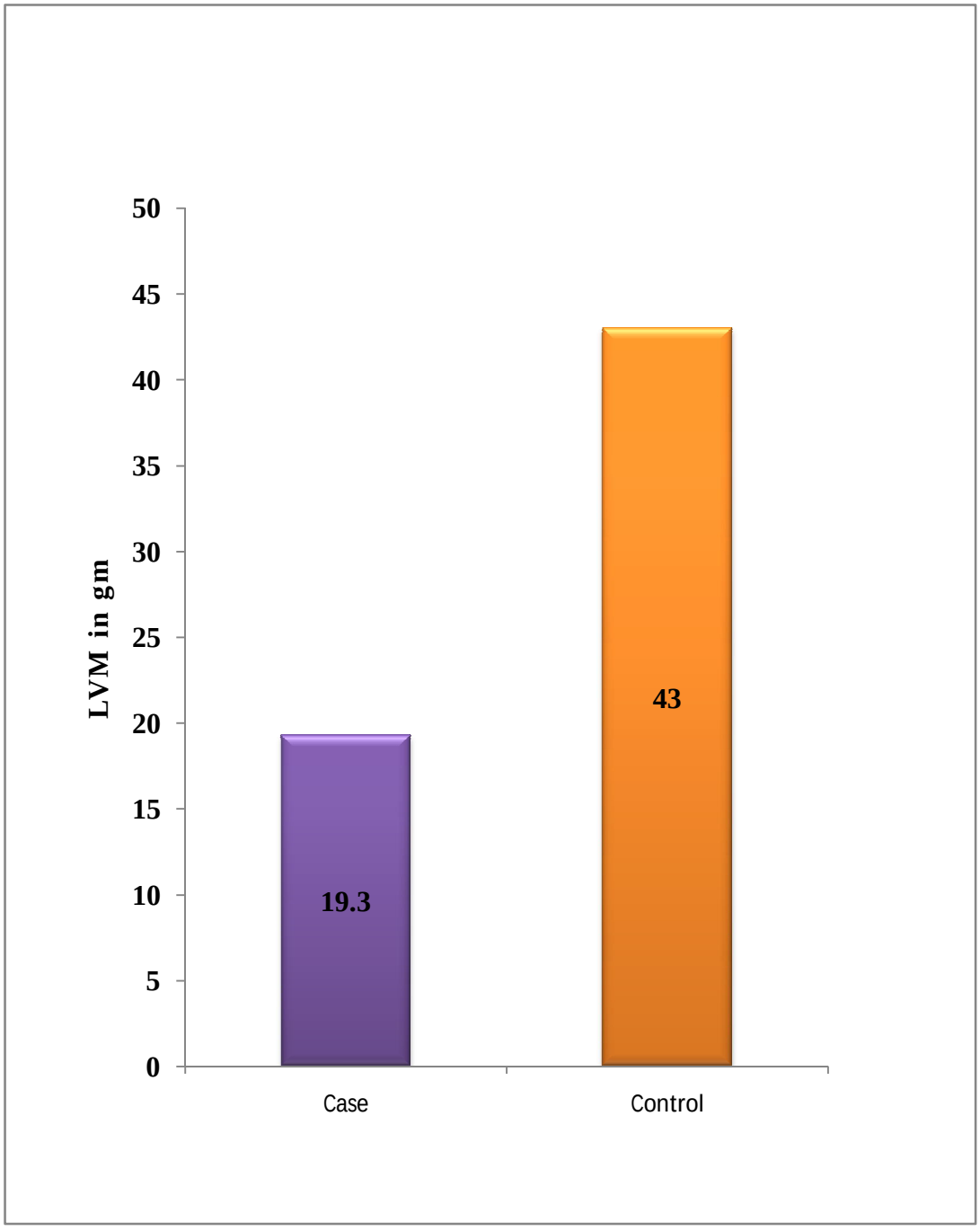
COMPARISON OF E/A RATIO BETWEEN CASE AND CONTROL

LEFT VENTRICULAR MASS

Mean left ventricular mass in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in left ventricular mass. Mean left ventricular mass of the children with severe acute malnutrition is 19.341. The mean left ventricular mass of the children in control group is 43.048. Mean left ventricular mass of the children with severe acute malnutrition is significantly lower than their matched controls (P< 0.001).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
LVM (g)	Control	21	43.048	12.9749	< 0.001
	Case	41	19.341	7.8823	

Table: 13 Left ventricular mass in case and control



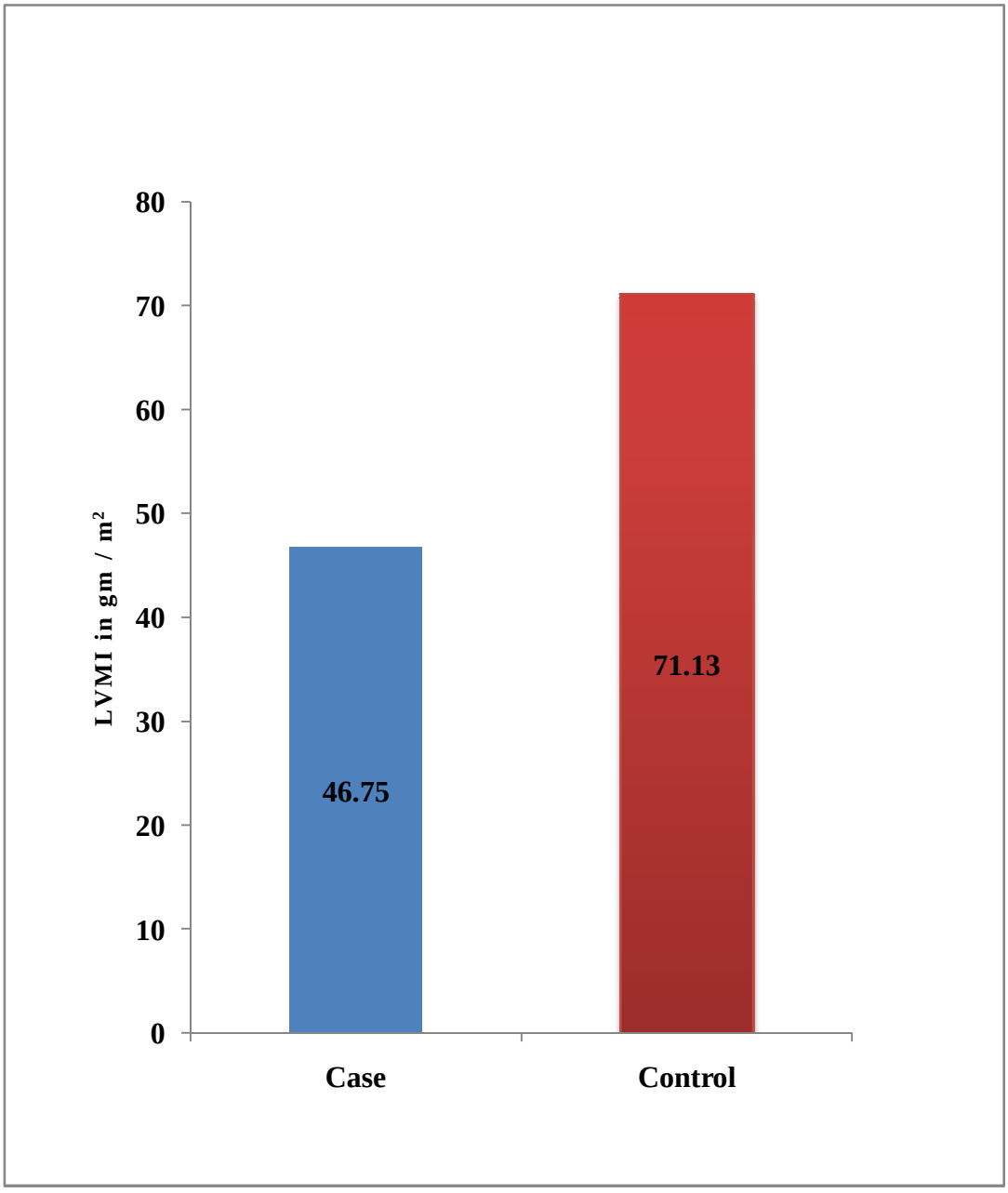
COMPARISON OF LEFT VENTRICULAR MASS BETWEEN CASE AND CONTROL

LEFT VENTRICULAR MASS INDEX

Mean left ventricular mass index in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in left ventricular mass index. Mean left ventricular mass index of the children with severe acute malnutrition is 46.756. The mean left ventricular mass index of the children in control group is 71.133. Mean left ventricular mass index of the children with severe acute malnutrition is significantly lower than their matched controls (P< 0.001).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
LVMI (g/m2)	Control	21	71.133	10.6336	< 0.001
	Case	41	46.756	15.3847	

Table: 14 Left ventricular mass index in case and control



COMPARISON OF LEFT VENTRICULAR MASS INDEX

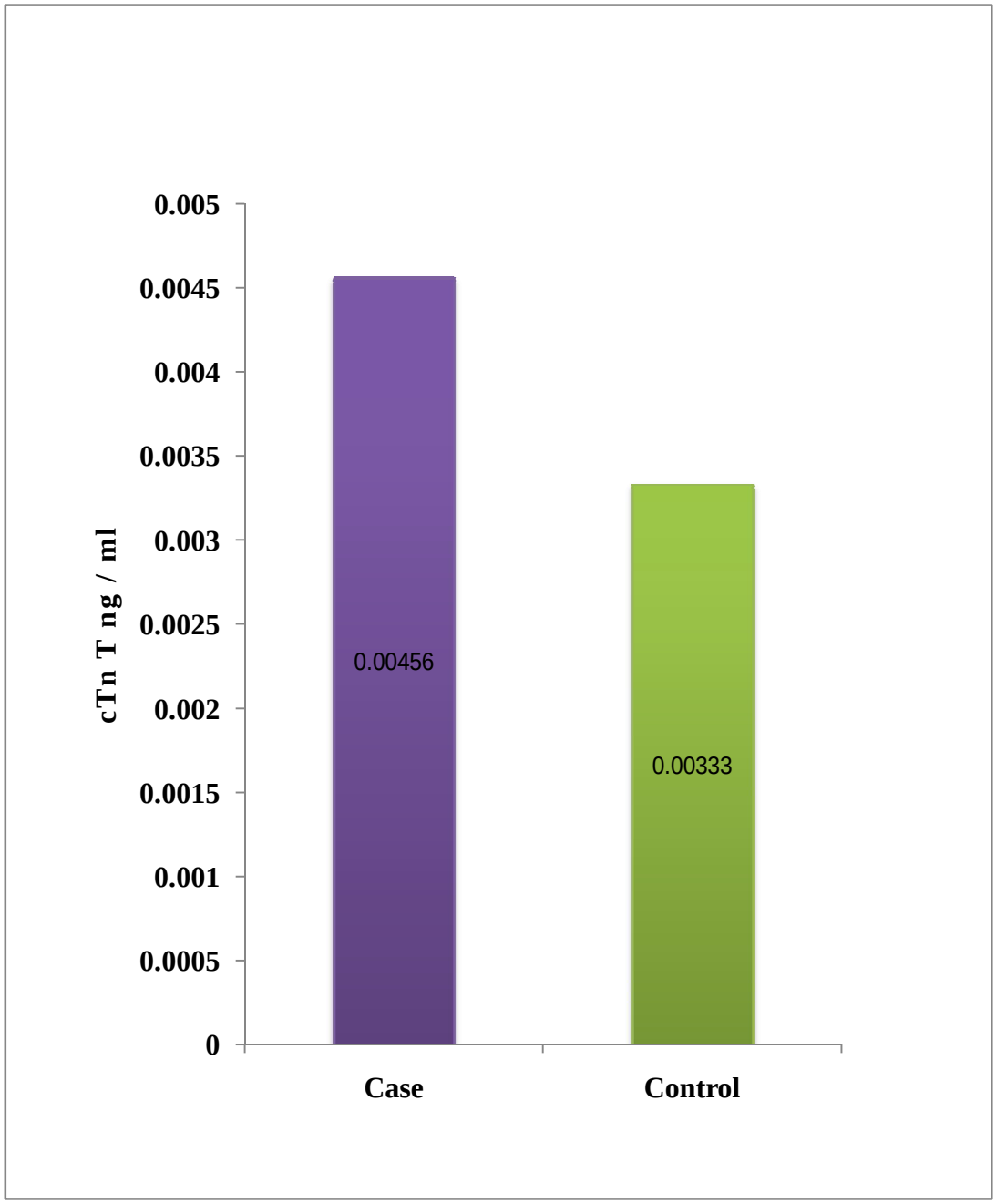
BETWEEN CASE AND CONTROL

CARDIAC TROPONIN T

Mean cardiac troponin T level in children with severe acute malnutrition is compared with their control group. There is no significant difference between children with severe acute malnutrition and controls in the cardiac troponin T level. Mean cardiac troponin T level of the children with severe acute malnutrition is 0.00456ng/ml. The mean cardiac troponin T level of the children in control group is 0.00333ng/ml. Mean cardiac troponin T level of the children with severe acute malnutrition is not significantly lower than their matched controls (p= 0.055).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
cTnT (ng/ml)	Control	21	0.00333	0.001683	0.055
	Case	41	0.00456	0.002599	

Table: 15 Cardiac troponin T level in case and control



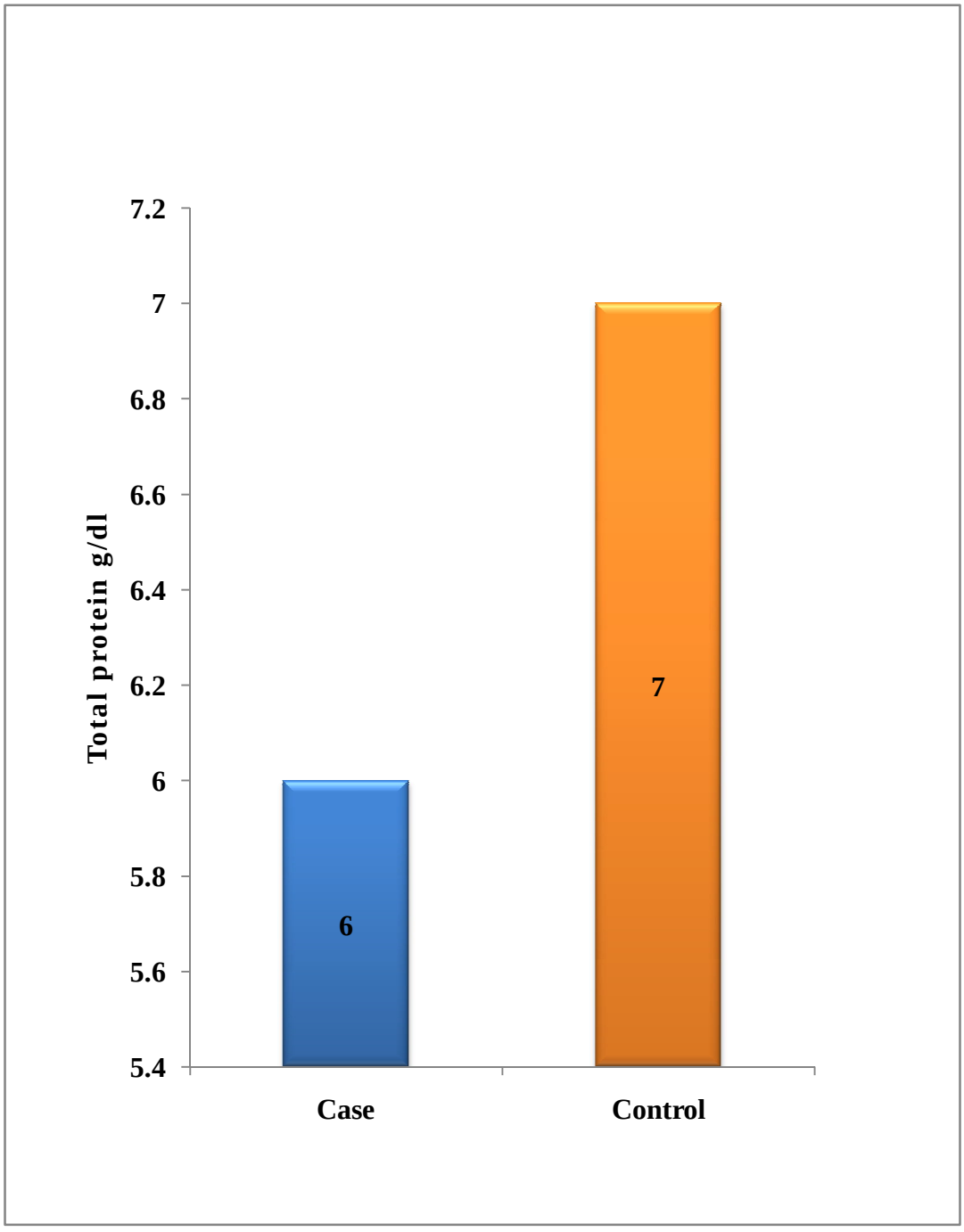
COMPARISON OF CARDIAC TROPONIN T BETWEEN CASE AND CONTROL

TOTAL PROTEIN

Mean serum total protein in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in serum total protein. Mean serum total protein of the children with severe acute malnutrition is 5.954. The mean serum total protein of the children in control group is 7.038. Mean serum total protein of the children with severe acute malnutrition is significantly lower than their matched controls (P< 0.001).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
Total protein (g/dl)	Control	21	7.038	0.4873	<0.001
	Case	41	5.954	0.5025	

Table: 16 Serum total protein in case and control



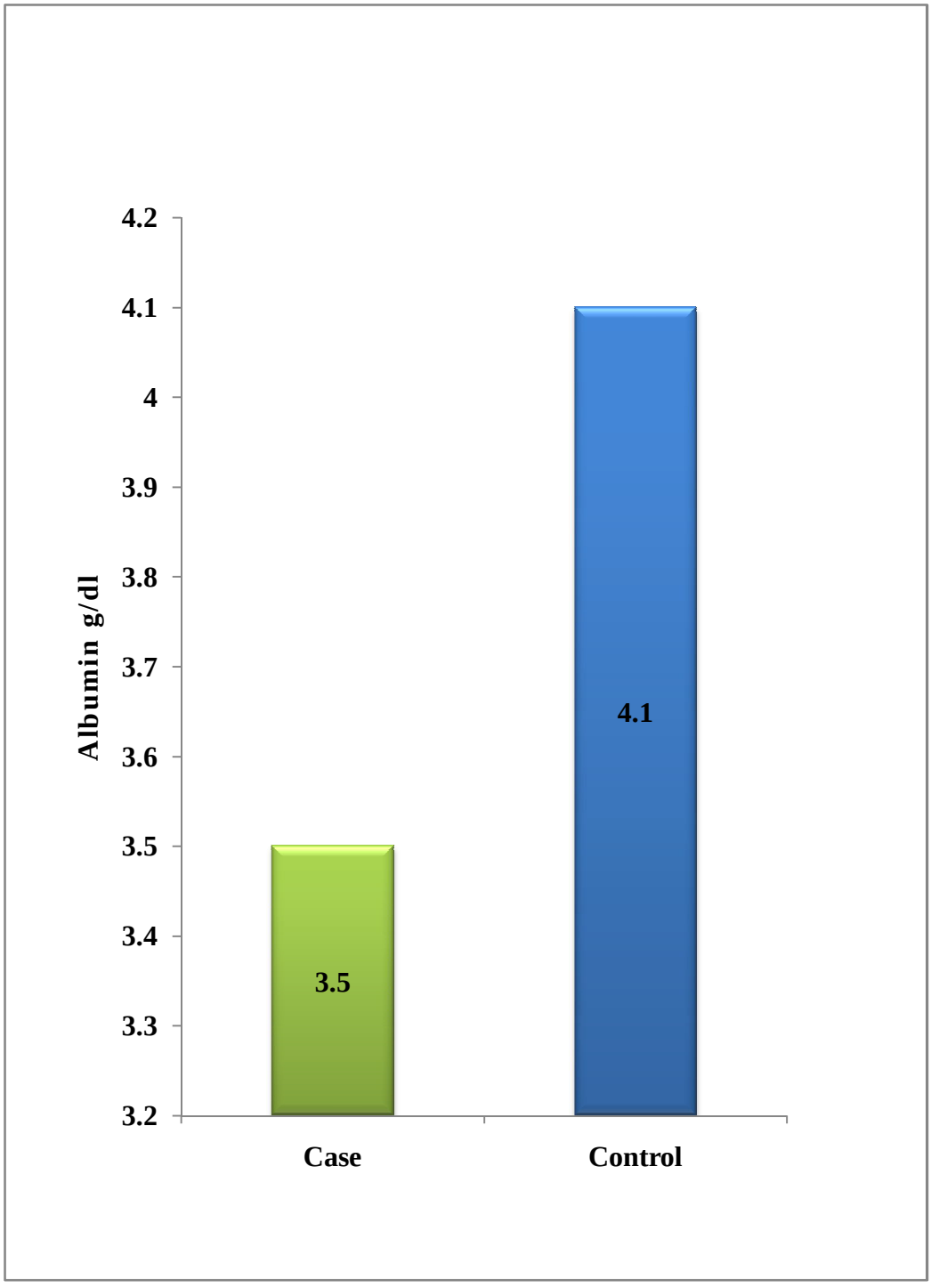
COMPARISON OF SERUM TOTAL PROTEIN BETWEEN CASE AND CONTROL

SERUM ALBUMIN

Mean serum albumin in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in serum albumin. Mean serum albumin of the children with severe acute malnutrition is 3.512. The mean serum albumin of the children in control group is 4.195. Mean serum albumin of the children with severe acute malnutrition is significantly lower than their matched controls (P< 0.001).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
Albumin (g/dl)	Control	21	4.195	0.4201	<0.001
	Case	41	3.512	0.4069	

Table: 17. Serum albumin in case and control



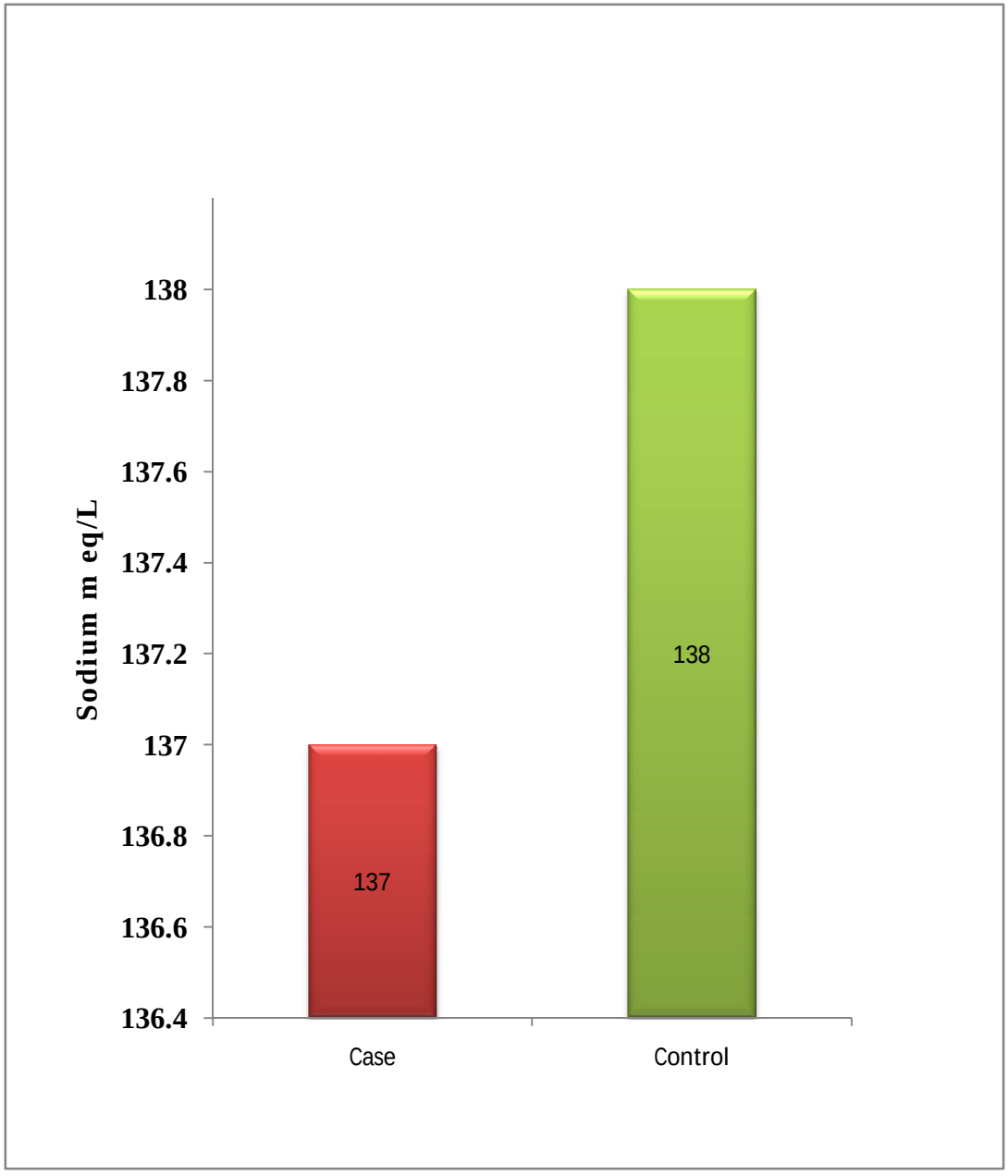
COMPARISON OF SERUM ALBUMIN BETWEEN CASE AND CONTROL

SERUM SODIUM

Mean serum sodium level in children with severe acute malnutrition is compared with their control group. There is no significant difference between children with severe acute malnutrition and controls in the serum sodium level. Mean serum sodium level of the children with severe acute malnutrition is 137.585 m eq/L. The mean serum sodium level of the children in control group is 138.476 m eq/L. Mean sodium level of the children with severe acute malnutrition is not significantly lower than their matched controls (p=0.140).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
Sodium (m eq/L)	Control	21	138.476	2.4417	0.140
	Case	41	137.585	2.0973	

Table: 18 Serum sodium level in case and control



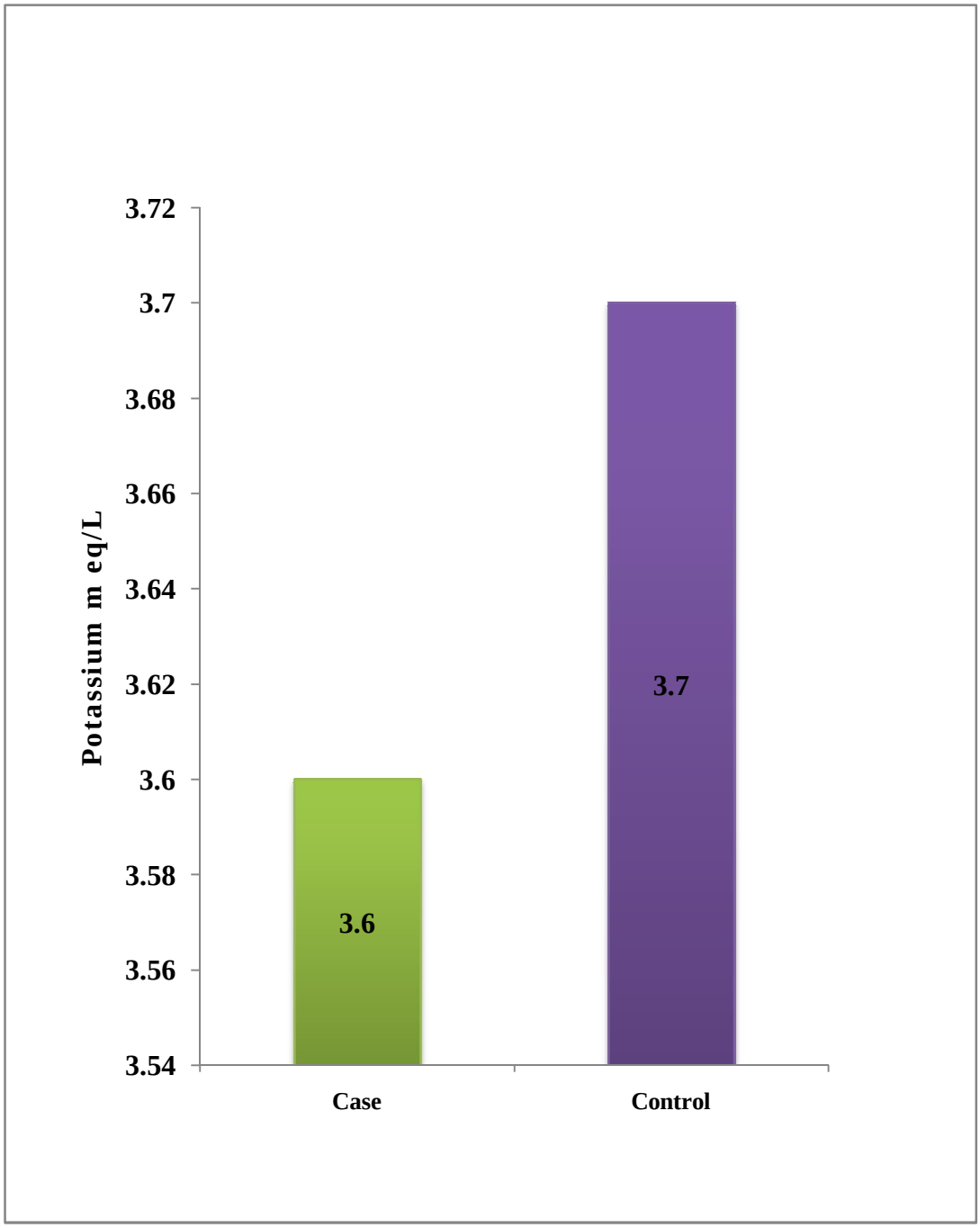
COMPARISON OF SERUM SODIUM BETWEEN CASE AND CONTROL

SERUM POTASSIUM

Mean serum potassium level in children with severe acute malnutrition is compared with their control group. There is no significant difference between children with severe acute malnutrition and controls in the serum potassium level. Mean potassium level of the children with severe acute malnutrition is 3.683 m eq/L. The mean serum potassium level of the children in control group is 3.781 m eq/L. Mean serum potassium level of the children with severe acute malnutrition is not significantly lower than their matched controls (p=0.105).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
Potassium (m eq/L)	Control	21	3.781	0.1940	0.105
	Case	41	3.683	0.2344	

Table: 19 Serum potassium level in case and control



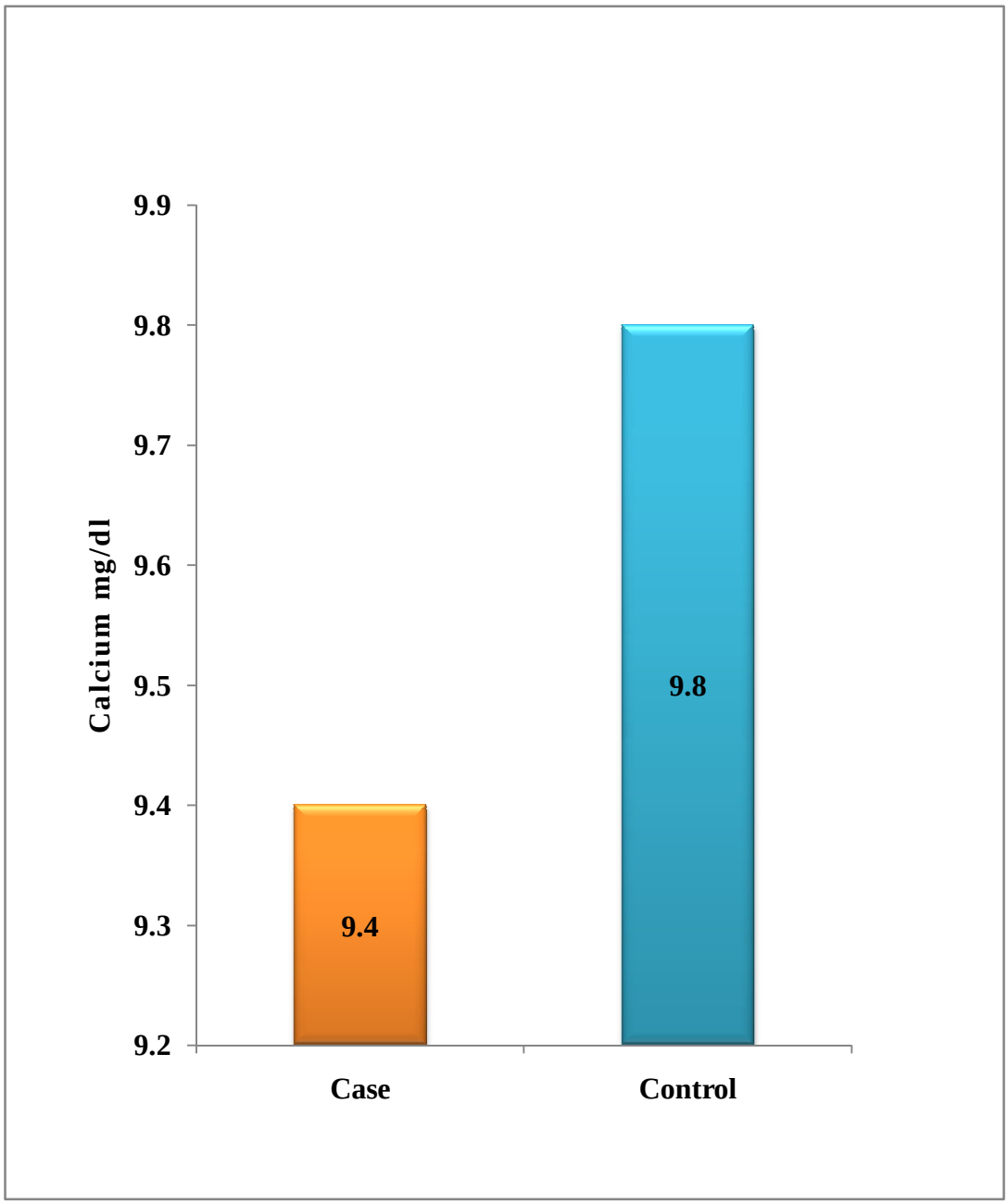
COMPARISON OF SERUM POTASSIUM BETWEEN CASE AND CONTROL

SERUM CALCIUM

Mean serum calcium level in children with severe acute malnutrition is compared with their control group. There is no significant difference between children with severe acute malnutrition and controls in the serum calcium level. Mean calcium level of the children with severe acute malnutrition is 9.456mg/dl. The mean serum calcium level of the children in control group is 9.838 mg/dl. Mean serum calcium cardiac level of the children with severe acute malnutrition is not significantly lower than their matched controls (p=0.067).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
Calcium (mg/dl)	Control	21	9.838	0.7413	0.067
	Case	41	9.456	0.7756	

Table: 20 Serum calcium level in case and control



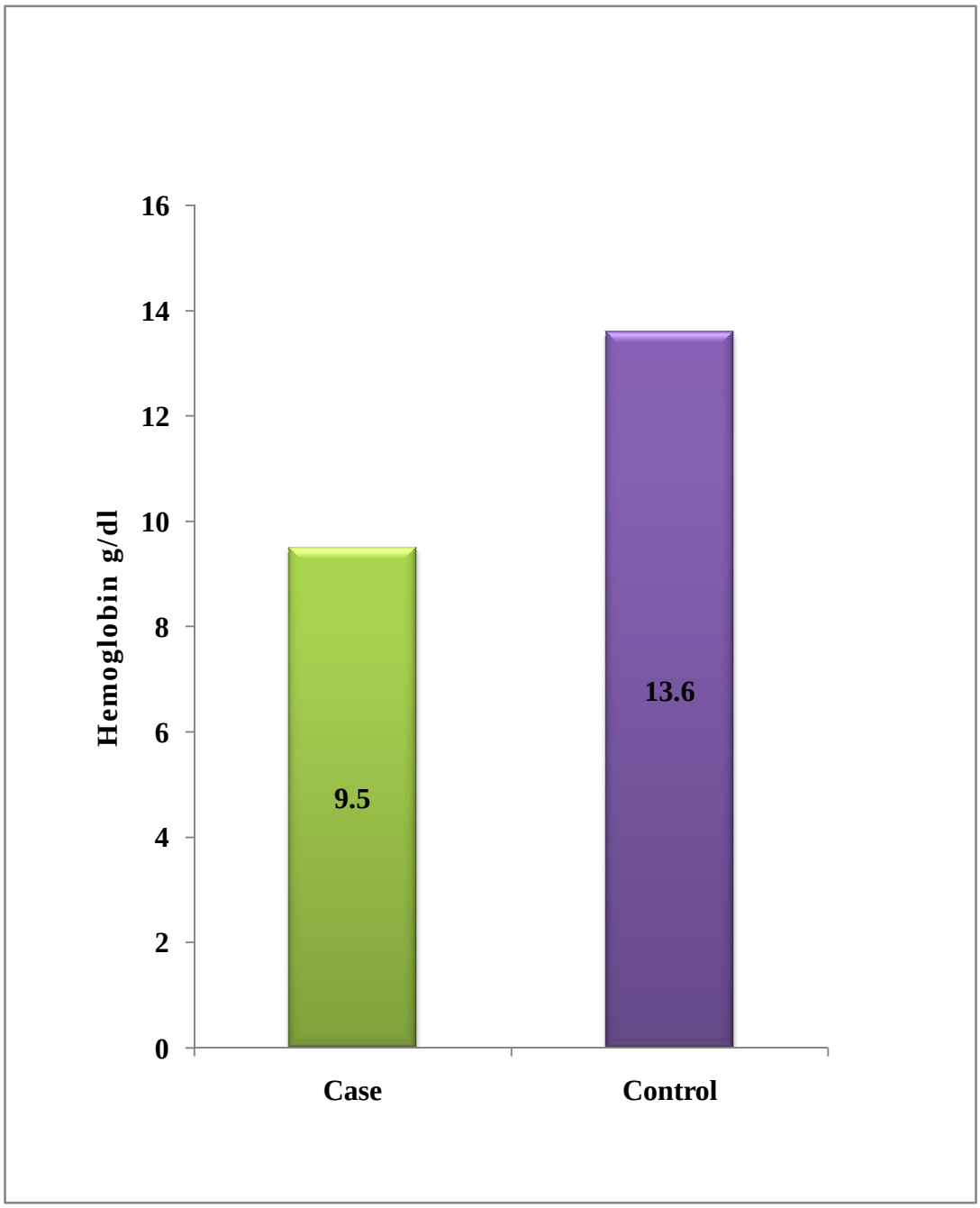
COMPARISON OF SERUM CALCIUM BETWEEN CASE AND CONTROL

HEMOGLOBIN

Mean hemoglobin in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in hemoglobin. Mean hemoglobin of the children with severe acute malnutrition is 9.546. The mean hemoglobin of the children in control group is 13.619. Mean hemoglobin of the children with severe acute malnutrition is significantly lower than their matched controls (P< 0.001).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
Hemoglobin (g/dl)	Control	21	13.619	0.5278	<0.001
	Case	41	9.546	0.9721	

Table: 21 Hemoglobin in case and control



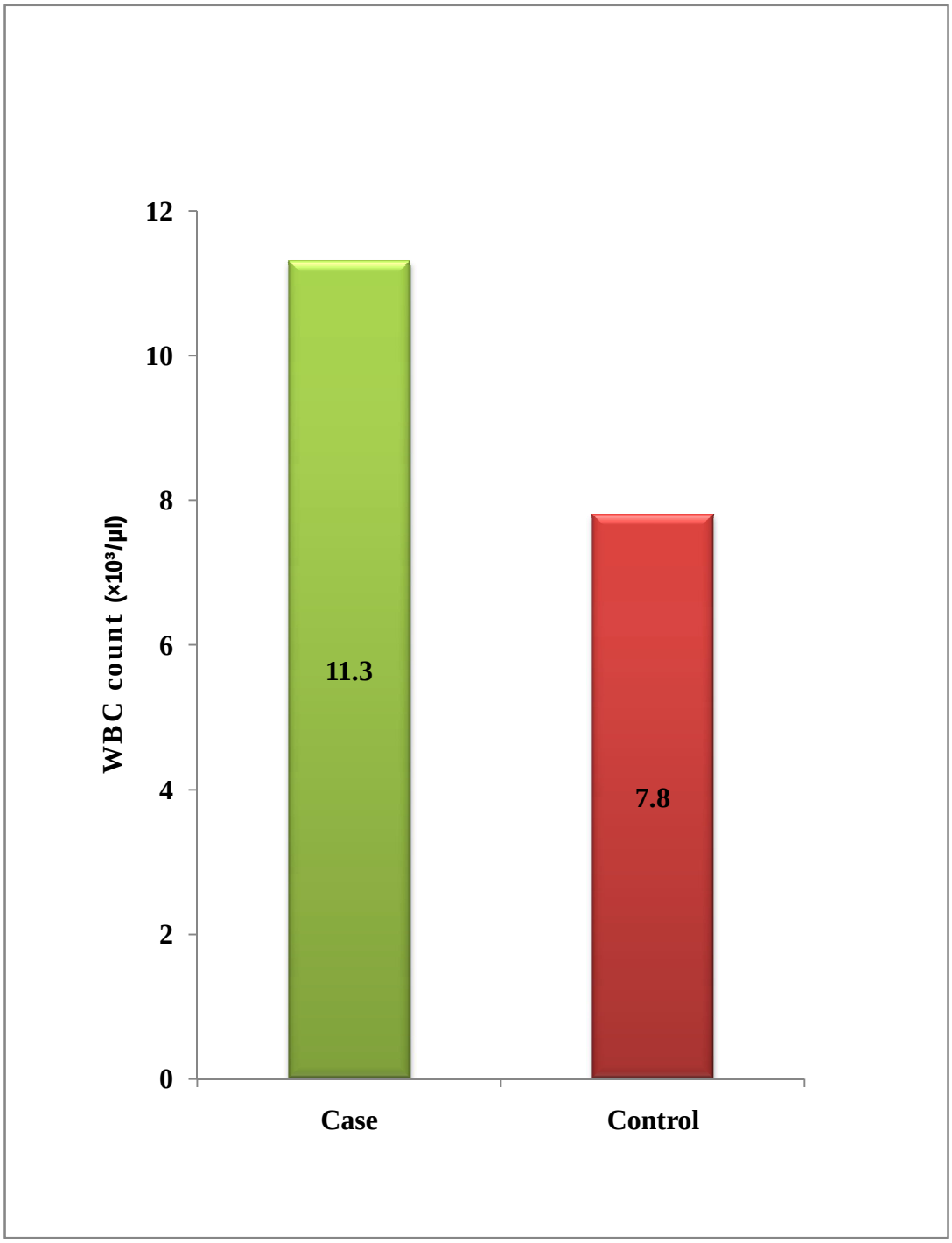
COMPARISON OF HEMOGLOBIN BETWEEN CASE AND CONTROL

WHITE BLOOD CELL – TOTAL COUNT

Mean WBC count in children with severe acute malnutrition is compared with their control group. There is a significant difference between children with severe acute malnutrition and controls in WBC count. Mean WBC count of the children with severe acute malnutrition is 11.293. The mean WBC count of the children in control group is 7.819. Mean WBC count of the children with severe acute malnutrition is significantly increased than their matched controls (P= 0.006).

	Group	**N**	**Mean**	**Standard Deviation**	**P value**
WBC ($\times 10^3/\mu l$)	Control	21	7.819	1.2855	0.006
	Case	41	11.293	5.5268	

Table: 22 WBC count in case and control



COMPARISON OF WBC COUNT BETWEEN CASE AND CONTROL

DISCUSSION

Severe acute malnutrition is a serious disease responsible for increased mortality and morbidity among children (under five age group) in developing countries. Echocardiographic evaluation of children with severe acute malnutrition in the present study showed left ventricle end diastolic diameter, end systolic diameter, thickness of posterior wall and interventricular septum were significantly decreased than healthy control group ($p<0.001$). The left ventricular mass and left ventricle mass index calculated from the above parameters were significantly decreased in children with severe acute malnutrition compared to control group.

This finding is similar to study done by Abu Faddan et al, who described echocardiographic evaluation done in 45 malnourished children, which revealed severe acute malnutrition children had reduced left ventricular mass and left ventricular mass index parameters.

HL El Sayed et al also noted findings similar to our study results, cardiac evaluation was done in 30 protein energy malnutrition children including both edematous and non edematous children before and after nutritional rehabilitation. Reduced left ventricle mass index observed in malnourished children significantly increased after nutritional rehabilitation.

J W Bergman et al, did echocardiographic study in 21 kwashiorkor children, out of which 81% had values below the 5^{th} percentile for

interventricular septal thickness, 71% had value less than 5th percentile for left ventricle posterior wall thickness.

The present study showed parameters of left ventricular systolic dysfunction (ejection fraction and fractional shortening) were not significantly decreased in children with severe acute malnutrition.

HL El Sayed et al described left ventricle systolic function indices (fractional shortening, ejection fraction and velocity of circumferential fiber shortening) were not significantly decreased in children with protein energy malnutrition compared to healthy control group.

Ocal et al reported no significant difference in systolic parameters (fractional shortening and ejection fraction) between malnourished children and healthy control groups.

Kothari SS et al, noted left ventricle systolic function parameters (fractional shortening, ejection fraction percentage and velocity of circumferential fiber shortening) were not significantly different in malnourished children than healthy controls.

On the contrary, Naggla Hassan abu faddan et al, who reported children with protein energy malnutrition had significant left ventricular systolic dysfunction than healthy control group. But there was no significant diastolic dysfunction in children with protein energy malnutrition compared to control group. Our study population had significant diastolic dysfunction compared to control population.

The current study shows left ventricle diastolic dysfunction as evidenced by reversal of mitral valve E/A ratio, pulmonary vein and hepatic vein pulse doppler in children with severe malnutrition compared to healthy control group. Diastolic dysfunction may precede the systolic dysfunction.

Singh GR et al described left ventricular dysfunction in moderate to severe protein energy malnutrition.

On the contrary, Abu Fadden et al reported no diastolic dysfunction with severe protein energy malnutrition when compared to normal healthy controls. Similar findings were also noted by HL El Sayed et al, Ocal et al in their studies.

Fioretto et al noted there is geometric alteration of left ventricle with preserved ventricular compliance and distensibility.

The present study shows cardiac troponin T level is not significantly increased in children with severe acute malnutrition compared to normal healthy children.

But Abu Faddan et al reported cardiac troponin T level is higher than upper reference value in children with severe acute malnutrition.

According to HL El-Sayed et al out of 30, only two severely malnourished children had detectable levels of cardiac troponin I in their serum.

Troponin T is a contractile protein found almost solely in the myocardium. It is only detectable at 4hour or more post acute myocardial injury but the condition is different in malnutrition.[10]

The malnourished individuals have lighter hearts but a greater Heart weight/Body weight coefficient than well nourished children. This finding indicates a possible preservation of myocardium in relation to the intensity of weight loss.[10]

Therefore malnutrition is slow myocardial anabolic rate rather than increased catabolism as in acute myocardial necrosis.10

STUDY LIMITATIONS

Co-morbid conditions like sepsis, micronutrient and vitamin deficiencies influence the cardiac functioning in severe acute malnutrition.

Further follow up study of these malnourished children is needed after the nutritional rehabilitation, which would suggest cardiac dysfunction due to malnutrition and its improvement with nutritional rehabilitation.

SUMMARY

Children with severe acute malnutrition have significantly reduced left ventricular mass and left ventricle mass index when compared to age, sex matched controls.

Severely malnourished children have significant left ventricle diastolic dysfunction compared to normal healthy children. But left ventricle systolic function is not significantly decreased compared to healthy controls.

There is no significant difference in serum cardiac troponin T in children with severe acute malnutrition compared to healthy control group.

CONCLUSION

Children with severe acute malnutrition have significantly reduced cardiac muscle mass, diastolic dysfunction but systolic function is relatively preserved compared to control group. There is no significant difference in serum cardiac troponin T level between these two groups.

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ஆராய்ச்சி ஒப்புதல் படிவம்

பெயர் : தேதி :

வயது : மருத்துவமனை எண் :

பாலினம் ஆராய்ச்சி சேர்க்கை எண். :

ஆய்விடம் : அரசினர் குழந்தைகள் நல மருத்துவமனை, எழும்பூர், சென்னை மருத்துவ கல்லூரி

ஆய்வாளர் : மரு. சா. செந்தில்ராஜா

1. இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் எனக்கு முழுமையாகவும், தெளிவாகவும் விளக்கப்பட்டது.
2. எனக்கு விளக்கப்பட்ட விவரங்களை நான் புரிந்து கொண்டு, எனது குழந்தையை இந்த ஆராய்ச்சிக்கு உட்படுத்த சம்மதிக்கிறேன்.
3. இந்த ஆராய்ச்சியின் தன்மைகளும், எனது உரிமைகளும் எடுத்துரைக்கப்பட்டது.
4. அதிகளவு ஊட்டச்சத்து குறைபாடுள்ள குழந்தைக்கு, இருதயத்தின் செயல்பாட்டுத் திறனை கண்டறியும், இந்த ஆய்வில் எனது குழந்தையை பங்கு பெற சம்மதம் தெரிவிக்கிறேன்.
5. நான் எனது குழந்தையின் முந்தைய மற்றும் தற்போதைய மருத்துவ விவரங்களை ஆய்வாளரிடம் தெரிவித்து விட்டேன்.
6. இந்த ஆய்வினால் ஏற்படும் ஆபாயங்களைப் பற்றி எனக்குத் தெரிவிக்கப்பட்டது.
7. எனக்கு குழந்தையின் உடல்நலம் பாதிக்கப்பட்டாலோ (அ) வழக்கத்திற்கு மாறாக நோய்குறி தென்பட்டாலோ உடனே அதை ஆய்வாளரிடம் தெரிவிப்பேன் என உறுதியளிக்கிறேன்.
8. நான் எனது குழந்தையை இந்த ஆய்வில் தன்னிச்சையாக எந்த நிர்பந்தம் இன்றியும் பங்கேற்க அனுமதிக்கிறேன். எந்த காரணத்தினாலும், எந்த காலக்கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இந்த ஆய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.
9. நான் இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும், அதை பிரசுரிக்கவும் என முழுமனதுடன் சம்மதிக்கிறேன்.

பெற்றோர் / பாதுகாவலரின் பெயர் ஆய்வாளர் கையொப்பம்

மற்றும் கையொப்பம் (மரு.சா.செந்தில் ராஜா)

தேதி :

இடம் :

INFORMED CONSENT FORM

Study place: INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN, PAEDIATRIC MEDICAL WARD AND NUTRITION OUT-PATIENT DEPARTMENT, CHENNAI.

Title of the study: **STUDY OF MYOCARDIAL DYSFUNCTION IN CHILDREN WITH SEVERE ACUTE MALNUTRITION .**

Name of the investigator : DR.S.SENTHIL RAJA

Name of the Participant: Age: Sex:

Hospital number: Blood sample no:

1. I have read and understood this consent form and the information provided to me regarding the participation of my child in the study.

2. I have had the consent document explained to me.

3. I have been explained about the nature of the study.

4. I have been explained about my rights and responsibilities by the investigator.

5. I have informed the investigator of all the treatments taking or have taken in the past

including any native (alternative) treatment to my child.

6. I have been advised about the risks associated with my child participation in this study.*

7. I agree to cooperate with the investigator and I will inform him/her immediately if my child suffer

unusual symptoms. *

8. My child have not participated in any research study in the past.

10. I am aware of the fact that my child can opt out of the study at any time without having to give any reason

and this will not affect my child future treatment in this hospital. *

11. I am also aware that the investigator may terminate my child participation in the study at any time, for

any reason, without my consent. *

12. I hereby give permission to the investigators to release the information obtained from my child as result

of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I

understand that they are publicly presented.

13. I have understand that my child's identity will be kept confidential if my child's data are publicly presented

14. I have had my questions answered to my satisfaction.

15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing

this consent form I attest that the information given in this document has been clearly explained to me

and understood by me, I will be given a copy of this consent document. For adult participants:

Name and signature / thumb impression of the participant /parents/guardian

Name _____ Signature_____ Date_____

Name and Signature of impartial witness:

Name _____ Signature_____ Date_____

Name and Signature of the investigator or his representative obtaining consent:

Name _____ Signature_____ Date_____

Data Collection Sheet

Date:

Sample no:

Case / Control

1.	Name	
2.	Age	
3.	Sex	Male/female
4.	IP/OP no	
5.	Parent/Guardian's name	
6.	Address	
7.	Socio-economic status	
8.	Symptoms Not gaining weight or height Fever Recurrent diarrhea Recurrent LRI/Ear discharge Recurrent UTI Edema of the body Skin lesions (exanthem)	 Yes/no Yes/no Yes/no Yes/no Yes/no Yes/no Yes/no Yes/no
9.	Developmental history	Normal/developmental delay
10.	Immunization history	

11. Diet history

	Intake	Expected	Deficit
Calories			
Protein			

12. Clinical examination

Mental state	Alert/dull
Emotional state	Comfortable/irritable/apathetic
Edema	Generalized edema/pedal edema

13. Clinical signs of malnutrition (jellife)

Hair	Flag sign
Face	Dyspigmentation Moon face
Eyes	Pale conjunctiva Bitot's spot Keratomalacia
Lips	Angular- palpebritis / stomatitis
Tongue	Atrophic papillae
Teeth	Mottled enamel
Gums	Bleeding gums
Glands	Thyroid / parotid enlargement
Skin	Flaky - paint dermatosis Pellagrous dermatosis
Nails	Koilonychia
Muscular and skeletal systems	Muscle wasting Craniotabes Frontal and parietal bossing Epiphyseal enlargement-tender/ non tender Beading of ribs Wide open af Knock knees/bow legs

14. Vital signs

HR - /min	BP - mmHg
RR- /min	Temp - F

15. Anthropometric measurements

Indicator		
Weight (in kg)		
Height/Length (in cm)		
Weight for Height		
MUAC		

Lab investigations

16. Echocardiography (2D Echo)

1.	Left ventricle Diastolic dimension Systolic dimension Posterior wall thickness	(in mm)
2.	IVS thickness (Diastolic)	
3.	Ejection fraction (EF %)	
4.	Fractional shortening (F/S %)	
5.	Lv diastolic funtion (E/A)	
6.	Left ventricle mass(LVM) Left ventricle mass index(LVMI)	

17. Cardiac troponin T

Value :	Normal Elevated

18. Serum proteins (in gms)

Total	
Albumin	
Globulin	

19. Serum electrolytes

Sodium		m eq/L
Potassium		m eq/L
Bicarbonate		m eq/L
Calcium		mg/dl

20. Others

Blood sugar	
Hemoglobin	
Total count	
Polymorphs	
Lymphocytes	
Eosinophils	
Platelets	
Culture -blood -urine	
Others (if any)	

21.

Chest X – ray (AP view)	

22. Conclusion

Myocardial function	Normal Abnormal Systolic / Diastolic dysfunction (if abnormal)
Left ventricular mass & Left ventricular mass index	Normal /Reduced
Cardiomyocyte damage	Present / Absent

MASTER CHART
CASE

SL.NO.	NAME	AGE (months)	SEX	Wt (kg)	Ht (cm)	MUAC	EDD (cm)	ESD (cm)	PWD (cm)	LVSD (cm)	EF (%)	FS (%)	E/A Ratio
1	Jeyalakshmi	2	F	5.9	79	11.2	2.47	1.68	0.34	0.34	62	33.3	0.765
2	Bhavani shankar	2	M	6.6	71	11.3	2.32	1.61	0.35	0.43	60	30.8	2.2
3	Ajay	1	M	6	69	11.2	2.46	1.45	0.23	0.31	74	41.3	1.72
4	Kumaran	2	M	8.8	84	11.2	3.5	2.25	0.35	0.55	68.7	35.7	1.68
5	Durga devi	1	F	5.8	68	11.2	2.3	1.33	0.43	0.53	75	41.9	1.57
6	Dhivaneshwaran	2	M	7	75	11	2.41	1.44	0.3	0.37	73.1	39.4	1.52
7	Rajeshwari	3	F	8	82	11.3	3	2	0.33	0.35	65.6	33.3	1.74
8	Velmurugan	3	M	6.5	78	10.2	1.95	1.18	0.29	0.32	73.4	39.5	1.62
9	Devi	3	F	9.4	90	11.4	2.94	1.86	0.34	0.39	70	36.7	1.77
10	Sarathy	3	M	9.1	87	11.3	3.6	2.5	0.42	0.45	61.8	30.6	1.63
11	Charmi	2	F	9	83	10.5	3.1	2.1	0.35	0.53	64.1	32.3	1.65
12	Sukanya	3	F	9	88	11.1	3.4	2.3	0.37	0.4	64.2	32.4	1.68
13	Kanimozhi	3	F	8.3	85	11.3	3.1	2.1	0.35	0.38	64.1	32.3	2.1
14	Usha	3	F	8.5	87	11.2	2.88	1.92	0.31	0.35	65.6	33.3	1.72
15	Radhika	3	F	8	82	11	2.75	1.81	0.27	0.31	66.7	34.2	1.65
16	Kavin	2	M	7.2	76	10.5	3.2	2.25	0.27	0.27	60.6	29.7	1.22
17	Malarvizhi	3	F	8.3	8.4	11.3	2.84	1.85	0.29	0.34	67.6	34.9	1.63
18	Gopinath	2	M	8	81	11.2	3.2	2.2	0.38	0.42	62.7	31.3	2
19	kiruthika	3	F	8.2	85	10.4	2.82	1.83	0.28	0.33	67.9	35.1	1.82
20	Priyadharshini	3	F	9.4	90	9.4	3.9	2.7	0.4	0.43	62.1	30.8	1.9
21	Venkatesh	2	M	6.1	70	10.3	2.89	2.05	0.3	0.31	59.7	29.1	1.34
22	Balaji	3	M	9	88	11.2	3.7	2.6	0.41	0.44	60.6	29.7	1.9

23	Maragatham	3	F	7.8	80	10.8	27	18	0.28	0.32	65.6	33.3	1.78
24	Vinoth	3	M	9	85	11.4	3.5	2.4	0.41	0.44	63	31	1.8
25	Selvam	1	M	5.5	68	11	2.83	1.88	0.29	0.3	64	33.6	1.3
26	Musthafa	3	M	8.2	83	10.8	2.5	1.7	0.29	0.34	63.8	32	1.62
27	Tharani	1	F	4.2	60	-	2.62	1.84	0.34	0.32	58	29.7	1.55
28	Saran	2	M	6	70	11.2	2.2	1.58	0.32	0.4	58.4	28.2	1.72
29	Sabiya	1	F	6.2	72	11	2.88	1.86	0.43	0.45	66	34.1	1.46
30	Kumar	3	M	8.8	87	11	2.7	1.9	0.31	0.35	60.5	29.6	1.82
31	Shalini	2	F	6	73	11.2	2.4	1.57	0.32	0.33	67.2	34.6	1.83
32	Sathyan	3	M	8.8	90	10.8	2.75	1.83	0.31	0.33	65.7	33.5	1.72
33	Madhu sree	1	F	6.1	70	10.7	2.63	1.78	0.3	0.32	64.2	32.3	1.32
34	Gowtham	2	M	8	80	10.5	2.56	1.75	0.34	0.34	62	31.6	1.7
35	Mukunthan	1	M	5.8	67	10.7	2.5	1.5	0.25	0.32	74	40	1.68
36	Ravi	3	M	10.2	92	10.2	3.15	2.13	0.35	0.38	64.3	32.4	1.64
37	David	3	M	9.2	89	11.2	2.85	1.95	0.32	0.36	63.2	31.6	1.72
38	Sanjana sri	2	F	8	81	11	2.8	1.8	0.31	0.51	65	35.6	1.63
39	Kannan	2	M	7	75	11	2.97	2.13	0.24	0.25	58.6	28.3	1.37
40	Pradheepa	1	F	4.36	61	-	2.22	1.35	0.32	0.34	73	39.2	1.58
41	Narayanan	3	M	9.1	88	11	2.9	2.05	0.34	0.37	60	29.3	1.81

LVM (g)	LVMI (g/m2)	cTnT (ng/ml)	TOTAL PROTEIN (g/dl)	ALBUMIN (g/dl)	Na (m eq/L)	K (m eq/L)	Ca (mg/dl)	Hb (g/dl)	WBCs (×10³/µl)
14	39	0.015	4	2.2	137	2.6	5.8	10.8	40.5
15	42	0.007	5.6	3.8	137	3.8	8	9.8	7
11	32	0.009	5.8	3.5	136	3.5	9.2	8.8	11.6
36	79	0.003	6.2	3.7	139	3.6	9.1	9.5	7.3
19	58	0.004	6.2	4	139	3.7	9.7	8.7	9.9
14	35	0.005	5.7	3.7	134	3.8	9.2	8.5	11.2
20	46	0.005	6.6	3.6	139	3.8	9.7	10.6	7.1
8	22	0.007	5.8	3.7	140	3.6	9.3	10.2	13.2
21	42	0.002	6.2	3.5	141	3.7	10.2	9.8	10.6
36	77	0.003	6.3	3.7	134	3.9	9.1	10.5	5.7
28	62	0.002	6.2	3.6	137	3.6	9.4	9.5	11.1
28	60	0.005	6.2	3.6	138	3.8	9.2	8.8	11.5
23	51	0.002	6.4	3.8	138	4.1	9.7	9.8	12.3
18	39	0.006	5.7	3	140	3.5	8.8	7.8	12.9
14	33	0.006	5.6	3.2	139	3.8	10.8	9.2	12.4
17	43	0.003	5.7	3.8	138	3.7	10.2	8.2	19.2
16	37	0.002	6.4	3.8	141	3.8	9.6	10.4	5.6
27	63	0.007	6.6	3.7	138	3.9	9.7	10.4	11.2
16	35	0.007	5.8	3.2	138	3.5	9.6	9.2	8.7
39	81	0.003	6.5	3.5	136	3.7	9.1	10.5	9.9
16	47	0.001	5.4	3	134	3.6	10	7.8	16.8
37	79	0.006	6.8	3.8	135	3.6	9.2	11.2	10.4
14	34	0.006	6.1	3.4	139	3.7	9.7	9.7	6.6
33	72	0.006	6.8	4.2	137	3.8	10.2	10.7	9.2
15	47	0.001	6	4.1	135	3.8	8.8	9.6	9

13	30	0.006	6.2	3.4	138	3.7	9.6	10.6	11.8
15	57	0.005	6.1	3.6	136	3.5	9.2	9.6	8.9
12	36	0.003	6.1	3.5	139	3.8	9.2	8.6	11.2
25	71	0.004	5.4	2.5	136	3.6	9.8	9.4	12.3
16	34	0.002	5.5	3	135	3.6	10.2	11.2	9.8
13	36	0.002	6.2	3.8	136	3.8	9.8	8.7	10.3
16	33	0.002	6	3.4	137	3.8	9.8	9.5	11.5
14	41	0.004	5.6	3.4	140	3.7	9.8	8.3	13.1
15	35	0.004	5.7	4	141	3.8	10.2	10.2	10.8
12	36	0.004	5.8	3.6	137	3.8	9.7	9.1	10
23	45	0.006	6.4	4.2	140	3.7	9.6	8.8	9.9
18	38	0.005	5.8	3.5	138	3.6	9.6	10.8	5.4
22	51	0.006	6.2	3.5	135	3.6	9.2	9.2	18
14	36	0.004	5.6	3.1	142	4	9.7	7.2	9
11	42	0.001	5.1	3.2	136	3.2	8.8	10	8.9
19	41	0.006	5.8	3.2	136	3.9	10.2	10.2	11.2

MASTER CHART
CONTROL

SL.NO.	NAME	AGE (months)	SEX	Wt (kg)	Ht (cm)	MUAC	EDD (cm)	ESD (cm)	PWD (cm)	LVSD (cm)	EF (%)	FS (%)	E/A Ratio
1	Prabakaran	2	M	15.5	95	14.2	3.82	2.58	0.51	0.53	64.4	32.5	1.8
2	Karunya	3	F	16.5	98	14	3.74	2.48	0.52	0.53	66	33.7	2.2
3	Sneha	2	F	14	94	13.8	3.66	2.43	0.47	0.49	65.9	33.6	2
4	Velvizhi	3	F	16.4	101	14	3.76	2.5	0.52	0.54	65.8	33.5	2.3
5	Nagaraj	2	M	11.6	84	13.6	3.51	2.3	0.46	0.46	67.1	34.5	1.57
6	Vanathi	3	F	17	103	14.2	3.78	2.47	0.54	0.54	67.3	34.7	1.7
7	Arun	2	M	13.8	93	14	3.76	2.53	0.5	0.5	64.7	31.4	1.57
8	Kavitha	2	F	11	79	13	3.15	2.12	0.37	0.39	64.7	32.7	1.58
9	Sivakumar	3	M	18	105	14.5	3.98	2.6	0.6	0.6	67.3	34.7	1.8
10	Priyanka	2	F	12.7	85	13.6	3.54	2.37	0.47	0.48	65.2	33.1	2.1
11	Saravanan	2	M	11.2	82	13.2	3.42	2.25	0.43	0.44	66.7	34.2	2
12	Laurence	3	M	19.2	108	15	4.12	2.63	0.64	0.62	69.3	36.2	2.3
13	Pandiyan	2	M	13.2	90	13.6	3.68	2.46	0.48	0.48	65.3	33.2	1.59
14	Sathish	1	M	10	78	13.8	3.3	2.2	0.41	0.42	65.6	33.3	1.57
15	Aravind	2	M	16.4	97	14	3.86	2.58	0.54	0.55	65.3	33.2	2.1
16	Kiruthika	2	F	11.4	85	13.6	3.46	2.34	0.44	0.45	64.3	32.4	1.56
17	Kathiravan	1	M	9	70	-	2.9	1.9	0.38	0.38	67.1	34.5	1.56
18	Vinitha	3	F	18.4	106	14.5	3.85	2.49	0.56	0.57	68.2	35.3	2.2
19	Anitha	1	F	9.5	71	-	3.1	2.1	0.4	0.4	64.1	32.3	1.59
20	Nandhini	2	F	15.6	96	13.7	3.68	2.45	0.49	0.5	65.7	33.4	2.1
21	Sabari	2	M	12.6	88	13.8	3.65	2.48	0.47	0.48	63.8	32.1	1.58

LVM (g)	LVMI (g/m2)	cTnT (ng/ml)	TOTAL PROTEIN (g/dl)	ALBUMIN (g/dl)	Na (m eq/L)	K (m eq/L)	Ca (mg/dl)	Hb (g/dl)	WBCs (×10³/µl)
50	78	0.004	7.6	5.1	135	3.8	10.7	13.6	7.9
49	72	0.003	6.5	3.8	137	3.8	10.7	14.2	5.9
42	69	0.003	6.7	4.1	142	3.9	10.4	14	7.1
50	73	0.002	7.8	4.9	136	3.7	10.5	13.6	6.2
37	71	0.003	7.5	4.7	142	3.9	9	13.8	6.4
51	73	0.005	6.7	3.9	140	3.7	10.3	14	7.6
46	77	0.001	6.2	3.7	139	3.8	9.1	14.1	9.6
24	50	0.002	6.8	4.1	140	3.7	9.1	13.8	7.2
64	88	0.004	7.3	4.5	135	3.5	10.5	13.8	8.1
39	71	0.002	7.6	4.3	137	3.5	8.9	13.6	8.7
33	65	0.002	7.6	4.2	137	4	9.7	12.5	8
72	95	0.001	6.5	3.9	139	3.7	10.7	13.7	6.6
42	74	0.007	6.4	3.8	142	3.5	8.8	13.8	9.1
29	63	0.002	7.2	4	137	4.1	9.4	13.5	11
54	81	0.006	6.8	4.1	139	4	10.7	13.8	7.3
35	67	0.003	7.3	4.6	140	3.7	8.9	14.2	8.9
21	50	0.002	7.2	4.2	136	4.2	9.6	12.5	9
56	76	0.003	7.6	4.2	137	3.8	10.5	13.8	8.3
25	58.8	0.004	6.5	3.5	143	3.8	9.2	13	6
44	68	0.005	7.3	4.7	139	3.8	10.6	14.1	7.5
41	74	0.006	6.7	3.8	136	3.5	9.3	12.6	7.8